Toric IOLs
J.L. Alio
Spain

Astigmatism as a refractive error can be visually disabling affecting the quality of vision and life of many patients. Approximately 18%-23% of cataract patients have ≥ 1.5D of preexisting astigmatism, 8%-10% of the population present ≥ 2.25D and approximately 2% present astigmatism ≥ 3.00D. Advances in the ability to correct the refractive errors of cataract patients with astigmatism have gained interest over the recent years.

Different surgical procedures exist to correct astigmatism at the moment of cataract surgery, such as limbal relaxing incisions (LIRs), astigmatic keratotomy, photorefractive keratectomy (PRK), and laser assisted in situ keratomileusis (LASIK). The advantages and limitations of these procedures have been well documented. For incisional refractive surgery, the results are variable and are dependent on the incisions’ depth and length, the size of the optical zone, the patients’ age and type of astigmatism. The skill of surgeon is as important. Likewise, the risk of over or under correction, perforation and wound gap also need to be considered. The cost of excimer laser is a major disadvantage. Complications, even that infrequent, such as loss of best corrected visual acuity, a decenttered ablation zone, flap complications, night vision difficulties and regression must be kept in mind.

In addition, all techniques, the amount of cylinder that can be corrected is limited. For this reason, in cases of high astigmatism, these procedures are associated with poor visual quality and low predictability.

The introduction of toric intraocular lenses provides an opportunity for a more precise correction of astigmatism. The concept of corneal decentration using astigmatism was first developed by Shimizu in 1992, the same year in which Grabow and Shepherd implanted the first foldable silicone toric plate haptic IOL. For one to achieve successful surgery with a toric lens, appropriate selection of IOL power and adequate rotational stability are essential to avoid the induction of astigmatism and to reduce preexisting astigmatism.1-11

In summary, the implantation of a toric IOL is an option for astigmatic correction at the time of cataract surgery for the following reasons:

1. It preserves the corneal integrity by avoiding alteration into the stromal lamellae therefore; there is no risk of regression. It’s safe and the results are more predictable.
2. The technique is a second option for the surgeon if in case there is a refractive error, the IOL can be repositioned or replaced to achieve astigmatic correction.
3. It’s a simple procedure; the surgeon doesn’t need a long learning curve.
4. This procedure doesn’t require special instruments or normograms.
5. It avoids surgically Induced astigmatism (SIA) and is effective in correcting high corneal astigmatism thus improving the quality of vision and life of the patients.

Symposium on the Treatment of Traumatic Optic Neuropathy Resolved: Corticosteroids Should Not Be Used
A. Arnold
USA

The treatment of indirect traumatic optic neuropathy (TON) has been controversial, especially since the natural history of the condition has been difficult to elucidate. Early series were biased toward more severe cases with poor prognostic for spontaneous recovery, while more recent literature includes a higher percentage with milder injury and better prognosis. In recent years, Lessell1 reported 5 of 25 untreated cases with subacute visual impairment. Seifert2, 5 of 15, Cook et al.11 49, and the International Optic Nerve Trauma Study (IONTS)5 57%, these data make attribution of visual improvement to a treatment modality more difficult. Moreover, the relative rarity of TON has relegated therapeutic reports to small case series, and the single major attempt at a randomized clinical trial of therapy (IONTS) was unsuccessful due to recruitment issues. The mechanisms of injury in central nervous system (CNS), and by extension, optic nerve trauma includes (mechanical disruption of tissue by shear or other force and 2. interruption of vascular supply), in which damage is immediate and probably irreversible; and secondary (1. vasospasm, 2. tissue swelling with compression within the optic canal, with axonal injury and further ischemia, and 3. subsequent cellular mechanisms including free radical production and excitotoxicity), in which damage develops later and theoretically may be prevented or mitigated. Such secondary injury is the focus of this review.

The mechanisms of action for corticosteroids in traumatic CNS injury include stabilization of the capillary membrane (reduction of extracellular edema), 2. anti-inflammatory, and 3. antioxidant and other proposed neuroprotective mechanisms. At lower and at so-called “high-dose” levels (eg 500-2000 mg/day methylprednisolone), membrane stabilization and anti-inflammatory effects probably predominate, while at “maga-dose” levels (eg > 4200 mg/day methylprednisolone), neuroprotective effects may come into play.

The use of corticosteroids in TON has been based on reports of benefit in CNS trauma. However, the well-documented beneficial effect of corticosteroids in reduction of edema in CNS neoplasms has been less rigorously documented in CNS injury. The North American Spinal Cord Injury Study (NASCIS I) showed no substantial benefit from standard dose corticosteroids after spinal cord injury. However, the NASCIS II did demonstrate that megadoses (4200mg/day), if administered during the 1st 8 hours after injury, resulted in improved long term function when compared to controls. Based in large part on these data, several studies were undertaken to assess a possible benefit of high or megadoses for TON. Anderson et al9 reported 3 of 6 cases improved after dexamethasone doses up to 200 mg/day. Seiff 10 reported visual improvement in 13 of 21 patients treated with 80 mg dexamethasone/day. Mauriello et al 11 reported 9 of 16 patients improved after 2000 mg methylprednisolone/day. 5400 mg/day, 40% of patients); dosage was not a significant obstacle to recruitment precluded its completion as a randomized clinical trial of therapy (IONTS) was unsuccessful due to recruitment issues. The mechanisms of injury in central nervous system (CNS), and by extension, optic nerve trauma includes primary (1. mechanical vascular supply), in which damage is immediate and probably irreversible; and secondary (1. vasospasm, 2. tissue swelling with compression within the optic canal, with axonal injury and further ischemia, and 3. subsequent cellular mechanisms including free radical production and excitotoxicity), in which damage develops later and theoretically may be prevented or mitigated. Such secondary injury is the focus of this review.

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The IONTS was developed to assess the benefit for visual outcome of corticosteroid treatment or optic canal decompression surgery versus observation. Although obstacles to recruitment precluded its completion as a randomized clinical trial as originally planned, the data obtained illuminated the lack of evidence for treatment effects for corticosteroids. In the 133 enrolled subjects, no significant differences were detected between the groups, with 57% of the untreated group showing increase in visual acuity by at least 3 Snellen lines versus 52% of those treated with corticosteroids. Treatment groups included 5 levels of therapy, ranging from "low dose" (<100mg methylprednisolone/day, 6% of patients), "moderate dose" (100-499 mg/day, 9% of patients), "high dose" (500-1999 mg/day, 19% of patients), "very high dose" (2000-5399 mg/day, 18% of patients), and "megadoses" (>5400 mg/day, 40% of patients); dosage was not a significant differentiating feature in visual recovery. The study concluded that although power was insufficient to allow comparisons between levels of treatment, that there was sufficient power for the overall treatment group (58% of which received > 2000 mg/day) to show that a beneficial effect was not demonstrated with corticosteroid therapy.

Moreover, the systemic risks of megadose corticosteroid therapy are well known, and include immunosuppression, psychosis, impaired glucose metabolism, and poor blood pressure control. Further, several reports of possible corticosteroid-induced CNS injury have surfaced. Lessell1 reported exacerbation of rat optic nerve axonal loss after crush injury with administration of high dose methylprednisolone vs control (saline).

Re-evaluation of the NASCIS I data suggested that administration after the 8 hour window could result in a worse prognosis. The CRASH (Corticosteroid Randomisation After Significant Head injury) study compared rate of death after
head injury in >10,000 patients treated with megadose (11.6 gram/day) methylprednisolone vs controls 10. Results indicated a significant increase in death risk at 2 weeks and in both death and disability at the 6 months following injury. While the cause of the increased death rate was unproven, the lack of benefit in reducing mortality and morbidity was clear. These conclusions were supported by other studies in the Cochrane Review 11 of 2009.

In summary, recent studies have shown:

a. That TON has a significant spontaneous improvement rate;

b. That evidence for improvement following corticosteroid use is based on small series with nonstandardized methodology;

c. That the largest and least methodologically limited study showed no benefit for the use of corticosteroids over observation; and

d. High dose and megadose corticosteroids may be harmful in CNS injury, including TON. We therefore cannot support the use of this treatment modality in TON.

REFERENCES


CLINICAL EXPERIENCE WITH THE CAPSULAR ANCHOR FOR SUBLUXED LENSES

E. Assia

Israel

Purpose: To describe the clinical results of patients implanted with the capsular Anchor in eyes with subluxated crystalline or intraocular lenses

Setting: Department of Ophthalmology, Meir Medical Center, Kfar-Saba, Israel.

Methods: The capsular Anchor is a PMMA device designed to treat lens subluxation caused by moderate to severe zonular dehiscence. The Anchor clips the anterior lens capsule and is sutured fixated to the scleral wall. Capsular tension ring (CTR) can be inserted in addition, to further stabilize the capsular bag.

Results: Ninety two eyes of 16 patients (3 bilateral, 11 males, mean age 44 years) with subluxated lenses of various etiologies (trauma, Marfan syndrome, primary ectopia lentis) were surgically treated using the Capsular Anchor. In one eye the capsular Anchor was used to treat subluxated IOL secondary to pseudoexfoliation. Surgical techniques were modified to accommodate lens position, length of zonular rupture or weakness and lens hardness. Capsular tension rings (CTR) were implanted in 4 eyes. In all cases the IOL remained central and stable for a follow up of over 3 years. No device related complications were recorded.

Conclusions: The Capsular Anchor is an effective means for treatment of subluxated lenses of various etiologies and severity.

WHAT IS THE FIRST-LINE TREATMENT OF MACULAR EDEMA IN DIABETES: CORTICOSTEROIDS

A. Augustin

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Diabetes mellitus, through its ophthalmologic complications, principally diabetic retinopathy (DR), is a leading cause of vision loss and blindness in industrialized nations. Despite the fact that significant advances are being made in early diagnosis and treatment of patients, numbers of patients likely to develop vision loss or blindness due to DR are expected to raise parallel to the incidence of diabetes. Underlying causes are the changing dietary habits leading to obesity as well as an overall increasing in ageing population. Estimates have projected that by 2050, there will be in excess of 50 million diabetics in the US, 50% of whom are projected to develop DR. In contrast to other underlying causes resulting in formation of macular edema (ME), such as RVO, the pathogenesis of diabetic macular edema (DME) is much more complex and multifactorial. DME can develop at any stage of DR, but it occurs more frequently as the duration of diabetes and the severity of DR increase. DME can be divided into a focal and diffuse form. Focal ME refers to localized areas of retinal thickening triggered by vascular abnormalities accompanied by fluid leakage and hard exudates. Diffuse ME is caused by a general diffuse leakage from dilated retinal capillaries throughout the posterior pole of the retina; it is commonly observed in both eyes.While there is also a classification of ischemic and exudative ME, hybrid types can be observed in most cases. Hyperglycemia -- the distinguishing feature of diabetes mellitus -- leads to serious cellular damage. Endothelial cells are extremely vulnerable to high glucose levels, which can seriously damage such cells and lead to DR. DR is characterized by abnormal vascular flow, hyperpermeability and leakage as well as non-perfusion of capillaries resulting in damage to retinal vasculature. Early stages of vasculature dysfunction are characterized by a breakdown of the blood-retinal barrier (BRB), leading to accumulation of fluid and serum macromolecules in the intercellular space and to loss of VA. Inflammatory components within the vascular tissue also play a central role in the development of ME. Several inflammatory mediators such as Angiotensin II, VEGF, prostaglandins, cytokines, ILS, VCAM-1 and ICAM-1 as well as macrophages and neutrophils are part of the local inflammatory process. To date, the complex chain of interaction of all these substances is not fully understood. However -as mentioned already - there is much evidence for the significant contribution of inflammation to the pathogenesis of this disease.

Spontaneous resolution of DME is rare and usually secondary to improvement in systemic risk factors such as glycemic control, hypertension or hypercholesterolemia. If left untreated, 29% of eyes with DME and foveal involvement experience moderate visual loss (doubling of visual angle) after 3 years. Spontaneous visual recovery is also unusual, with only 5% of cases experiencing an improvement of 3 EDTRS (Early Diabetic Retinopathy Study) lines. The diagnosis of DME is done clinically. The term ‘clinically significant macular edema’ characterizes the severity of the disease and provides a threshold to apply laser photocoagulation according to ETDRS. Control of systemic risk factors influences the course of DME. Several studies have clearly demonstrated that persistent hyperglycemia is strongly associated with the incidence and progression of ME. Especially, lower levels of glycosylated hemoglobin have turned out to be associated with a lower incidence of ME, independent of the duration of diabetes mellitus. Furthermore, systolic blood pressure, prevalence of diabetic nephropathy, smoking as well as hyperlipidemia was found to be associated with ME. While focal or grid laser photocoagulation has consistently shown efficacy in clinical trials, treatment is not without potential complications and new treatments are necessary for those who are either unresponsive to it or show less than ideal response.

To fulfill this unmet need, several pharmaceutical therapies are currently under development for DME. The majority are intravitreally injected anti-inflammatory or anti-angiogenic agents. The overall results of anti-VEGF drugs currently under investigation for efficacy and safety in DME are promising.
However, an obvious drawback is the frequency of having to inject which puts a great burden on patients suffering from this chronic disease. In addition, a frequent application of anti-VEGF drugs may be harmful to the neurosensory retina. Moreover, the class of anti-VEGF drugs is not performing a causal treatment rather than a temporary closure of the altered tight junctions. In contrast, by influencing the inflammatory cascade corticosteroids are acting in a more causal way.

Intravitreally applied corticosteroids at low dose have been observed to exert no relevant retinal toxicity. For quite a number of years, triamcinolone acetone has been used in ophthalmic practice as off-label injectable suspensions of between 4 and 20 mg. Differences in particle size may contribute to variability in clearance times and durations of action following intravitreal injections. Results of such preparations for the treatment of ME are far from ideal. In addition, the side effects of triamcinolone on IOP are sometimes dramatic and difficult to manage.

Non-biodegradable delivery systems releasing corticosteroids are also under clinical investigation for DME. However, the need to perform initial surgery rather than to do a simple injection as well as the need to remove the empty device could be considered a hurdle to usage. Also, concerns about side effects (of fluorocinolone) remain.

Although the biodegradable dexamethasone DDS is so far not yet approved for treatment of DME, it has shown most positive characteristics. Clinical experience is increasing because the drug is approved to the treatment of ME due to retinal vein occlusion and uveitis. Compared to other steroid systems, it is easier to apply and does not need to be removed. Compared to anti-VEGF drugs, it needs to be dosed more frequently which should lead to a better patient compliance and less injection-related risks and adverse events.

THE ROLE OF ADJUNCTIVE TREATMENT IN AMD

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Many treatment options are available for the management of choroidal neovascularisation secondary to age-related macular degeneration, yet no single treatment has been shown to permanently arrest the progress of the disease or to offer significant improvements in visual acuity. Although each therapy offers some unique benefit in terms of vision saved or loss of vision reduced, each has its limitations as well. All relevant monotherapies have drawbacks. The monotherapies cannot fully address the multifactorial pathogenesis of wet AMD.

The current viable monotherapies available to treat CNV were originally conceived as cancer treatments to arrest the neovascularisation that feed tumors before they were developed for and applied to ocular diseases. Similarly, combination therapy for ocular CNV was derived from the combination therapy concept in oncology. In both therapeutic areas, the goal of combination therapy is to disrupt the multiple stimuli that lead to pathological cellular proliferation. In case of cancer, both the tumor and the neovascularisations that feed the tumor are targets, while in ocular CNV, the neovascularisation itself is the target. Several known factors contribute to pathological CNV. The cascade of subretinal changes that leads to neovascularisation appears to take place as follows: ineffective metabolic activity [i.e. access of nutrients to receptors blocked and cellular waste clogging the tissue] leads to hypoxia; hypoxia leads to choroidal vascular atrophy; choroidal vascular atrophy leads to inflammation; inflammation leads to angiogenesis, and angiogenesis, mediated by VEGF leads to neovascularisation.

The vascular endothelial growth factor (VEGF) is expressed primarily in the endothelial cells of the vasculature. It is induced mainly by hypoxia, but also by radicals, cytokines, onkogenes and other growth factors. VEGF is the main trigger for new vessel growth, vasculogenesis (healthy vasculature) as well as angiogenesis (pathological vasculature) and induces inflammation and increases permeability of the vessels by a breakdown of the blood-retinal barrier (BRB).

The three main therapeutic targets of CNV development and proliferation, as shown in the cascade of subretinal changes already described, are neovascularisation itself, angiogenesis and inflammation.

If combination therapy is a more reasonable approach than monotherapy with anti-VEGF drugs, by applying this strategy we should be able to achieve:

1. A better visual outcome and/or
2. A reduction of treatments necessary.

So far not all prospective trials could “not definitively” show that combination therapy is superior or equal to anti-VEGF monotherapy while the RADICAL-study was in favour of combination therapy the MONT BLANC-study and the DENALI-trial investigation 255 and 300 patients could not clearly show this positive effect. On the other hand there are numerous trials which clearly show a benefit of combination therapy.

In addition, looking at the neovascularization and the three “anti’s”
- Anti-angiogenic (growing vessels)
- Anti-inflammatory (inhibits leukocytes, macrophages)
- Anti-fibrotic (inhibits fibroblasts)

a combination approach consisting of a CNV – eradicator, an anti-VEGF drug and an anti-inflammatory drug is reasonable.

Results of the MERLOT and the CABERNET trial add more information to the concept of eradicating the CNV. Preliminary observations suggest that a single procedure of epimacular brachytherapy reduced patients’ need for ongoing anti-VEGF therapy. Importantly, 63% of patients showed some improvement in visual acuity, with 50% gaining at least five letters or more at six months. A 50% reduction in the re-injection rate was noted as compared to the injection rates six months prior to receiving epimacular brachytherapy. With no single treatment able to address the complex multifactorial pathogenesis of wet AMD, combination therapies are now being intensely studied. Targeting different disease components with different therapies that have different mechanisms of action has more potential to successfully treat the numerous pathogenetic factors involved than any monotherapy. We still need more evidence from clinical trials which demonstrates the numerous potential benefits of combination therapy, including improved VA outcomes, lower re-treatment rates and longer treatment-free intervals. Therapy that will improve vision with as few administrations as possible, ideally in one cycle, while maintaining efficacy and tolerability is the goal. Triple combination therapy with a steroid, a CNV eradicator and an anti-VEGF agent now appears most capable of achieving this.

PRN ANTI-VEGF
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Anti-VEGF therapy for choroidal neovascularisation has revolutionized the approach to Age-related Macular Degeneration. While visual acuity improvement could be obtained in about one third of patients according to the results of multicentre trials, a meaningful socio-economic burden has been related to the therapy. The paramount treatment regimen should be a monthly anti-VEGF injection. It is also obvious that this regimen has clear practical limitations. Anti-VEGF therapies using variable injection regimens and combination therapies have emerged as alternatives to standard monthly monotherapy to address drug costs, patient risks, in association with office workload. Variable anti-VEGF regimens employ reduced-frequency intravitreal injections on an as-needed basis or a fixed intermittent schedule. Although high-level evidence available from randomized clinical trials generally indicates less favourable outcomes for variable anti-VEGF regimens, positive results from some prospective and retrospective studies support a reduced-frequency regimen.

Question 1
What is the best treatment regimen for anti-VEGF in AMD?

- monthly injection (correct answer)
- quarterly injection
- PRN

Question 2
PRN regimen is as effective as monthly injection in AMD?

- Yes (correct answer)
- No (correct answer)
CHARACTERISTICS AND IMPACT OF THE DIFFUSION OF MEDICAL TECHNOLOGIES

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Technological innovation in health care is an important driver of cost growth. Physicians and patients often embrace new modes of treatment before their benefits and shortcomings have been adequately investigated. Medical technologies can lead to increases in costs, either because they are simply more expensive than their predecessors or because their introduction leads to an expansion in the types and numbers of patients who will be eligible for treatment. We will discuss the medical technologies and the factors involved in their adoption, and describe robot-assisted surgery as one of the examples. The issues that will be addressed are cost-benefit, marketing and reimbursement forces, as well as the impact the adoption of certain medical technologies has had on the training of physicians and on clinical decision making processes.

OCULAR SURFACE SQUAMOUS NEOPLASIA (OSSN):
HOW TO TREAT – ALWAYS EXCISION, WITH OR WITHOUT ADDITIONAL TREATMENT
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Ocular surface squamous neoplasia (OSSN) comprises a wide spectrum of dysplastic alterations of the squamous epithelium of the surface of the eye, e.g. the conjunctiva and the conjunctival sleeve, ranging from “precancerous” lesions to bona fide invasive carcinoma. In the former case they are classified as carcinoma-in-situ lesions in conjunctival-corneal intra-epithelial neoplasia (CCIN) and in the later in invasive squamous cell carcinoma (SCC). The clinical presentation of Ocular surface squamous neoplasia (OSSN) varies across a wide spectrum and is classified based on the degree of epithelial and stromal infiltration. The epithelial infiltration can range from mild to severe dysplasia to full-thickness epithelial dysplasia (carcinoma in situ) and invasive squamous cell carcinoma, when tumor cells invade through the epithelial basement membrane and into the conjunctival and or corneal stroma.

Ocular surface squamous neoplasia (OSSN) can involve the conjunctiva or the cornea individually but more commonly start in the conjunctiva and extend across the limbus to involve the adjacent cornea. Various terms were used to describe these neoplasms, including epithelial plaque, Bowenoid epithelioma, and precancerous epithelioma. Pizzarello and Jakobiec proposed a terminology that parallels the gynecologic pathology terms for intraepithelial neoplasia. They classified conjunctival intraepithelial neoplasms as mild, moderate, and severe dysplasia based on the extent of involvement. Lesions that involve the basal one-third of the conjunctiva are classified as mild, those involving the inner two-thirds are classified as moderate, and lesions that are full thickness are termed severe dysplasia. OSSN is reported to be a relatively common neoplasm of the ocular surface, particularly in areas with high ultraviolet light B rays exposure. Other risk factors have been reported to be advanced age and male sex, mutation of the p53 tumor suppressor gene, immunosuppression in organ transplant recipients, smoking, and in some settings, HPV infection. In Africa, OSSN is lately more commonly reported. It seems to be more aggressive, and more likely to affect young people, especially females. In parallel with the dramatic increase of HIV in Africa, several countries have noted a sharp rise in the incidence of OSSN in HIV infected individuals. OSSN is currently the most common ocular tumor among adults in Africa.

Therapeutic options: Surgical excision is the traditional therapy for OSSN. Surgical excision involves excision of the lesion with wide surgical margins. Surgery can be followed by adjunctive cryotherapy to reduce the recurrence rate. Recurrence rates after surgical excision have been reported as high as 33% with clear surgical margins and up to 56% with positive surgical margins. Due to the reported high recurrence rates, adjunctive medical interventions for OSSN have been proposed. Local medical therapy has the advantage of treating the entire ocular surface, avoiding wide excision, which poses the risk of stem cell deficiency and long term ocular surface problems. Mitomycin C, 5-fluorouracil, and interferon alpha 2b have been found to be effective in the management of OSSN. IFNa2b drops are well tolerated and have minimal side effects. On the contrary Mitomycin C eye drops usually cause epithelial toxicity, reactive conjunctivitis, photophobia and severe discomfort. Therefore a local chemotherapy regime is usually preferred usually as one week on, and then one week off, that gives opportunity for corneal and conjunctival epithelial regeneration and recovery. IFNa2b drops generally are well tolerated when used 4 times daily until tumor resolution. A drawback to treatment with IFNa2b drops, however, is that the time to tumor resolution can be prolonged.

Reduction of recurrences with the post-operative use of topical mitomycin C has been published. Once the histopathological diagnosis of OSSN has been established after excision of the suspected lesions, adjuvant medical therapy is advised irrespective of whether or not the surgical margins are positive. It has been proposed that the presence or absence of positive surgical margins has no predictive ability with respect to the likelihood of developing recurrent tumors in the absence of adjuvant therapy. This suggests that equal concern is required for postoperative management of tumors that have been histopathologically been reported having clear margin resection (R0) and those having tumor infiltration in the resection margins (R1). The demonstration that adjuvant therapy with mitomycin C greatly reduces the recurrence rate in eyes with positive surgical margins and significantly reduces the recurrence rate in those with negative margins suggests that such treatment should be provided in all histopathologically confirmed cases of intraepithelial neoplasia. The intraoperative use of mitomycin C (such as in glaucoma surgery) has also been proposed to reduce the recurrence rate. This observation warrants further investigation in a prospective clinical trial before a recommendation can be made as to whether it should be replaced the postoperative use as the treatment of choice for this disorder.

Several reports have also confirmed the clinical efficacy of topical 5-FU in the treatment of preinvasive ocular surface neoplasia. The 1% dose of 5-FU used in clinical studies appears to be well-tolerated in the vast majority of patients. These authors used 5-FU four times daily for 14–21 day cycles with no long-term side effects. Medena demonstrated that topical chemotherapy with 5-FU alone was effective in eradicating OSSN in patients without major and/or long-term side effects. In addition, 5-FU may have a more favorable side effect profile than topical mitomycin C, although more studies are needed to validate this potential advantage.

References:
10. Chen HC, Chang SW, Huang SF. Adjunctive treatment with interferon alpha-2b may decrease the risk of papilloma-associated
conjunctival intraepithelial neoplasms or recurrent conjunctival intraepithelial neoplasms. The use of mitomycin C in the treatment of melanoma-positive intraocular tumors results in higher diagnostic accuracy compared to conventional methods. The use of mitomycin C in the treatment of melanoma-positive intraocular tumors results in higher diagnostic accuracy compared to conventional methods.

patients, 85% were phakic. High miopia was present in 14%. The primary outcome measure was anatomical reattachment of the retina with a single intervention (single operation success – SOS). Secondary outcome measures included postoperative visual acuity (VA) and postoperative complications. Results: Sixty-two (75%) patients achieved the SOS, with no significant differences between phakic and pseudophakic eyes. The eyes with RRD recurrence were treated with scleral buckle (48%) or pars plana vitrectomy (52%); all cases had anatomical success at final follow up. Postoperative VA improved in 60% of the SOS patient. The average duration of follow up was 14 months (range 3-38 months).

Conclusions: In this case series, pneumatic retinopexy was as effective for the repair of RRD as most large published reports. However, failure of pneumatic retinopexy could be successfully treated by scleral buckle or pars plana vitrectomy.

FUNDUS AUTOFLUORESCENCE IMAGING
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UK

AF is an intrinsic property of certain materials that is characterized by the transient emission of light when the substance is illuminated by an exogenous source. Many tissues and structures in the eye, such as the cornea, the crystalline lens and the retinal pigment epithelium are composed of biological molecules that have autofluorescent properties. Imaging of autofluorescent tissues has been exploited, particularly with regard to the fundus, where its relevance to disease is of considerable interest. The early imaging systems that were modified to detect fundus AF have since evolved into sophisticated, commercially available instruments such as the confocal laser scanning ophthalmoscope (cSLO). With increasing clinical use of such instruments, information on the topographic distribution and intensity of AF has accrued in both normal and diseased eyes. Thus it is important to examine critically the relevance of this information to the understanding of the biological significance of AF and its alterations with physiological ageing and in pathologic states.

The principles of physics as applied to the imaging of live tissues in the fundus are highly complex and create considerable potential for misinterpretation of findings. Perhaps the greatest challenge facing this potentially valuable tool is the lack of a standardized normative database and descriptors of disease developed from large longitudinal databases. Scrutiny of the evidence reveals not only a lack of a properly constructed and evaluated normative reference database of fundus AF, but also the corresponding absence of a comprehensive library of disease phenotypes. The terminology used to classify disease varies from one report to another, with different groups invoking different classification systems, often based on a relatively small number of patients. The absence of normative AF imaging databases makes it impossible to make robust age-matched comparisons between studies. This is an important issue because macular pigments vary with age and affect the measurement of fundus AF.

Developing true “norms” in AF imaging is likely to be difficult, as the RPE is a highly variable tissue, even within one individual. Although the RPE appears phenotypically regular, it is known that there is striking cell-to-cell variability in the content of melanin and lipofuscin granules, as well as in the expression of many proteins. The consequence is a tissue where variability in autofluorescence is to be expected and handling this in the context of disease is fraught with difficulties. Furthermore, none of the studies of AF has systematically examined reproducibility and consistency. Differences in photodetector gain and laser amplification between SLO devices could introduce variability into the data, parameters that are mandatory for an absolute comparison of AF images if data are to be combined. Thus a number of problems exist and has not been routinely addressed in the literature in AF imaging.

PRIMARY ACQUIRED MELANOSIS IS A MISNOMER AND SHOULD BE TREATED ONLY IF OF SIGNIFICANT RISK FACTORS EXIST
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Primary acquired melanosis (PAM) encompasses a wide range of conditions, which include benign and neoplastic melanocytic proliferation as well as non-neoplastic over-production of melanin by a normal population of melanocytes. Some advocate the use of PAM even for melanoma in situ and this is because of concerns about alarming the patient. Such vague terminology is therefore confusing and gives patients and healthcare practitioners a false sense of security. There is scope for more precise expressions, such as conjunctival melanocytic intra-epithelial neoplasia. Such disease tends to be described by adjectives such as ‘mild’, ‘moderate’ and ‘severe’, which are ambiguous. It would be preferable to use a scoring system based on melanocytic spread, density and atypia. It is this score, rather than extent of disease, that should guide therapy.

LARGE CONJUNCTIVAL MELANOMAS SHOULD BE TREATED BY EXCISION WITH ADDITIONAL THERAPY
B. Damato
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Conjunctival melanomas can seed around the conjunctiva, spread into orbit and nasolacrimal duct, and metastasize to the regional lymph nodes and systemically. Currently, most patients are treated by local resection, possibly with adjuvant cryotherapy. However, published series report high rates of local tumour recurrence. Such recurrent tumour can be difficult or impossible to control without extentionation and seems to increase the risk of metastatic disease. For this reason, I have for several years treated invasive conjunctival melanomas by surgical resection followed by radiotherapy, consisting of brachytherapy for bulbar tumours or proton beam radiotherapy for tumours involving the fornix, caruncle or tarsal conjunctiva. Such radiotherapy is administered even when histology suggests total excision. Diffuse intra-epithelial disease is treated with topical chemotherapy. These measures have achieved high rates of local tumour control, reducing the need for extentionation and possibly improving survival.

STRETCHING THE LIMITS OF EXCIMER LASER SURGERY: LASIK IN HIGH HYPEROPIA
D. de Ortueeta
Spain
The goal of the treatment in hyperopic LASIK surgery should be to change the slope of the cornea without inducing aberrations and this change should be stable over time.

Hyperopic LASIK has some pearls and this gives us the limitation that we should take into account to get good results:
1) The refraction as the patient has latent hyperopia which should be also corrected.
2) The centration which is still controversial. We advocate centring on the vertex normal of the cornea, a geometrical and reproducible point on the cornea.
3) The created flap exposing the stromal bed should be big enough for covering the total ablation.
4) The ablation profile was we should get smooth transition zones. As most of the ablation occurs at the middle periphery of the cornea we have two transition zones one to the not treated centre of the cornea and the second transition zone to the periphery of the cornea. If we have also astigmatism we will have a transition zone at the middle periphery. We need aspherical profiles and they should take into account that the laser spot efficacy diminishes at the periphery.
5) Regression: after a treatment the cornea is remodelling. New studies show that with an optical zone of 6.25 mm or larger we get stability at 3 months.
6) Biomechanical. The peripheral cornea should not be thinner than the central part of the cornea (inversion of pachymetry progression).
7) Postoperative keratometry reading not higher than 49 Dioptres.
As the laser technology has progressed, we put predictable results. Reviewing the results and taking into account the different parameters as postoperative keratometry and an optical zone of 6.25 mm or larger the upper limit of hyperopic LASIK will be about 6.5 to 7 Diopters in one meridian.
We have also learned from hyperopic Lasik that Presbyopic patients may benefit of inducement of negative spherical aberrations. New profiles use this information to treat presbyopia in hyperopic patients.

INCISIONAL BIOPSY OF THE IRIS
L. Desjardins
France

Malignant tumors can be located in the iris including iris melanoma, lymphomas and metastatic tumors. Indications of iris biopsies varies depending on the suspected tumors.
Most pigmented tumors of the iris are usually benign naevi. They often appear early in life and are slow growing tumors. They can produce ectropion of the uvea. Malignant iris melanomas usually appear in older patients. Nevertheless iris melanoma represents around 50% of uveal melanomas in young patients. They have a tendency to invade the ciliary body and to grow more rapidly. The typical signs of malignancy are seeding of pigment tumor cells in the angle distant to the main tumor and elevated intraocular pressure. It has been shown recently(1) that biopsy of pigmented iris lesions can lead to a falsely reassuring negative or inconclusive results. Modern management of iris lesions includes ultrasound biomicroscopy and treatment by proton beam of melanomas of the iris.
Decision of treatment is taken if there are 2 or 3 signs of malignancy and/or if the tumor is growing. This attitude avoids unnecessary esthetic and functional impairment observed after surgical removal of iris lesions.
For suspicion of iris metastasis or iris lymphoma it is sometimes necessary to confirm the diagnosis, this can be done either by fine needle biopsy or punch biopsy(2).

References:

LARGE CONJUNCTIVAL MELANOMA HOW TO TREAT?
L. Desjardins
France

Large conjunctival melanoma tends to deeply invade; thus it is impossible to totally remove them with sufficient security margin with conservative management of the globe as the deep border of the tumor is in contact with the globe. We have learnt from the dermatologist that a large removal is the key for local control but this is not possible with conjunctival melanoma if we want to preserve the eye.
So even if the pathologist finds a complete excision of the tumor, it is mandatory to use radiation therapy in addition to obtain a good local control.
Various type of radiation therapy has been used over the years including strontium applicators, plaque brachytherapy and external beam radiotherapy by photons and by proton beam. In the ideal situation, it is better to have all these techniques available as the best type of radiation varies according to the size and location of the tumor and also the age and general status of the patient.
In 1990 treatment by local excision followed by beta ray irradiation (Sr-90/Y-90) or cryotherapy was recommended as the treatment of choice by P lommatzsch(1) who had recommended this therapy in previous papers also(2)
Proton beam therapy of conjunctival melanoma was first described by Brovkina in 1987 (3) and Zografos in 1992(4).
In 1999 we have shown in a retrospective study of 56 patients a significant better prognostic for patients who received external beam radiation with photons in addition to surgery(5) but radiotherapy had been used for conjunctival melanoma since many years in our institution(6)
Iodine plaque brachytherapy of conjunctival melanoma was described by Stannard in 2000(7)
Due to the very small number of patients it is difficult to perform randomized study in this disease(8).
In our institution we treat all invasive conjunctival melanoma by complete surgical excision performed under general anesthesia followed by radiation therapy.
We use proton beam for most tumors involving the bulbar conjunctiva, iodine plaque brachytherapy for small bulbar conjunctiva not invading the cornea and external beam radiotherapy with photons for tumors of the lids or sulcus. In addition we perform TEP scanner and if positive results we use surgery and radiotherapy on regional lymph nodes and we treat all residual intra epithelial melanocytic proliferation with 0, 04% mitomycin drops two courses of 15 days.

References:
photographs and UBM data. 60% of the patients had documented growth of the tumor. The median diameter of the tumors was 5 mm. Careful examination of the angle was performed before iridectomy surgery and in case of abnormal pigmentation in the angle the planning of therapy was modified to include the involved angle in the field of radiation.

Two patients developed recurrence: one was retreated by proton beam and one was enucleated. One patient developed metastatic disease.

The main complication was cataract. Raised intraocular pressure was observed in 15% of patients but no neovascular glaucoma. These results are consistent with the literature[2]

In our experience most iris melanomas are localized lesions with invasion of the angle. Invasion of the angle can be found in a much greater area that of the visible mass. Instead of radiating the entire anterior chamber we think that it is justified to carefully discuss the planning of therapy with the physicist and to include in the field of radiation the tumor mass and the involved angle thus sparing the part of iris and anterior chamber that are free of tumor cells. Very few local recurrences are observed and this avoids the corneal procedure that is necessary to preserve limbal stem cells when the whole anterior segment is irradiated.

References:

LENS EXTRACTION IS THE PREFERRED TREATMENT OF PRIMARY ANGLE-CLOSURE GLAUCOMA

S. Foster

UK

Primary angle-closure glaucoma (PACG) is a surgical condition. The final common pathway is a physical obstruction of the trabecular meshwork by the peripheral iris. Peripheral iridectomy (PI), and later iridotomy, have remained the clinical cornerstone of management because they are quick, technically simple and work well in most cases. Interventional studies of PI using ultrasound biomicroscopic imaging have shown that 75% of people have a wider angle after PI than before. However, the same studies show that 59% of people undergoing PI have iridotrabecular contact (ITC) in more than one quadrant of angle (the consensus threshold for intervention in angle-closure disease).

Removal of a cataractous lens to improve visual function is one of the safest and most cost-effective health interventions available. Primary angle-closure (the bulk of angle-closure disease) occurs in eyes with an abnormally large and anteriorly positioned lens. These eyes typically are small, with axial length < 22.00mm. Removing the lens has an undoubtable impressive effect of increasing angle width. The increase in angle width is far greater than that seen after PI. Greve first proposed extra-capsular lens extraction as an alternative to filtering surgery in angle-closure in 1888. With the development of phaco-emulsification cataract surgery, there has been growing confidence in using lens extraction in cases with co-existent cataract. It has been shown that phaco for cataract combined with PACG improves visual acuity, reduces IOP, reduces the need for glaucoma medication (Lai, J Glaucoma 2006). Phaco will reverse ITC in all PACG eyes in the absence of aqueous misdirection syndrome or synechial closure, and results in profound widening of the angle. Further, audit of outcome of lens extraction surgery in PAC & PACG at Moorfields Eye Hospital, showed that the greatest benefit in terms of IOP lowering occurred in people with greater pre-operative pressures, more extensive synechial closure, worse glaucomatous optic neuropathy and those using the greatest number of medication. Laser iridotomy performs poorly in people with presenting IOP > 35mmHg, more than 6 clock hours of peripheral anterior synechiae, and in people with established glaucomatous optic neuropathy. Incidence and prevalence of PACG increase with age, meaning that most people suffering this condition are presbyopic, and have some nuclear sclerotic lens opacity. Lens extraction is therefore the preferred treatment for PACG.

SELECTIVE PERIMETRY IS OFTEN USEFUL

D. Friedman

USA

"Pre-perimetric" glaucoma is frequently present in clinical practice. What this means is that some patients lose ganglion cells but do not have evidence of damage on standard white-on-white perimetry. Significant worsening of the disease can occur without any identifiable changes in the visual field. Following patients in this early stage with white-on-white perimetry is not effective, and alternative approaches to testing are helpful. Frequency doubling technology can often identify patients as having visual field loss who do not demonstrate field loss using standard techniques. So too can alternative testing strategies such as short-wavelength automated perimetry ("blue-on-yellow"). Adding these selective perimetry approaches can result in better care of patients with concerning optic nerve head findings. Abnormalities on testing with them is predictive of later abnormalities on white-on-white perimetry.

Q1. What are alternative approaches to testing the visual field in patients with pre-perimetric glaucoma?

Correct = d

Q2. Persons with abnormalities on SITA SWAP testing:

Correct = c

Screening for glaucoma is justified: Glaucoma is an asymptomatic condition that results in progressive loss of visual function. Self-referral for vision loss due to glaucoma results in only the most advanced cases being identified (as is typically the case in many developing countries where over 90% of glaucoma cases are undiagnosed). Even in developed countries the rate of diagnosis of POAG is about 50% and among minority populations of Hispanics in the United States it was only 25% to 33%. Treatments have been proven effective in slowing the rate of progression of glaucoma damage. If unnecessary blindness is to be prevented, persons with asymptomatic disease must be identified. Screening can be done in the community or it can be done opportunistically or in a targeted fashion. While community-based screening may not be feasible at present, current technology allows us to identify subjects with glaucoma at relatively low cost provided the testing is applied intelligently. A combination of fast visual field testing and optic nerve imaging can identify the vast majority of those with glaucoma and also performs as well as or better than a clinician examining the patient. Provided appropriate logistics and attention to cost control, routine screening should be performed in high risk populations. Screening should be aggressively carried out in first-degree family members of persons with known glaucoma as they are at high risk. Similarly, certain populations are at substantial risk of glaucoma (such as Afro-Caribbean and older persons) and should be screened.

Q1. Siblings of those with POAG have an increased risk of POAG. This is about:

Correct = c

Q2. Screening in populations with low prevalence of disease requires a very high:

Correct = c
Angle closure is the result of multiple factors in these eyes, and iridotomy is generally safe and frequently effective and that it leads to better outcomes than iridotomy and medical hard to justify the risk of surgery without compelling evidence. Furthermore, cataract surgery can lower IOP.

Many antibiotics, such as those of the quinolone drug class, whose oral form is practically bioequivalent to the intravenous form, are available for the management of the most likely causes, such as Pseudomonas aeruginosa. Studies comparing the oral with the intravenous administration of the same or other antibiotics showed similar effects in the pharmacokinetics and management of infections. Moreover through oral administration complications associated with venous catheterization are avoided and the costs of therapy are considerably reduced. Subsequently oral antibiotics can be considered the primary treatment of choice for infective orbital cellulitis especially in cases of early disease (Stage I. or II. according to Chan’s classification) or in cases where factors implying high risk of complications are absent.

Q1: Treatment for primary angle closure glaucoma includes all of the following except
a. Observation
b. Laser iridotomy
c. Medical therapy
d. Cataract surgery
e. Trabeculectomy
Correct answer = a

ORAL ANTIBIOTICS ARE NOW THE PRIMARY TREATMENT OF CHOICE FOR INFECTIVE ORBITAL CELLULITIS: CON
M. Gonzalez-Candial
Spain

Orbital cellulitis is a medical emergency with potential vision and life threatening complications. Its aetiology includes spread from any infection, direct inoculation after surgery or trauma, acute dacryocystitis, bites, or haematogenous origin. Cultures should be obtained and antibiotic treatment started immediately.

I.V. antibiotic treatment have quicker action than oral antibiotic and, since many of these patients are children, it is also a more adequate way to confirm that the drug is administered and delivered at its appropriate dose, depending on the patient’s weight. A faster reaction to treatment can be observed with I.V. antibiotics and, if necessary, change to a different antibiotic therapy can also be achieved in a quicker way. If there is no improvement after 24-36 hours, surgical debridement and/or sinus surgery should be performed. CT scan with contrast is the study of choice. MRI can provide useful information, mainly if cavernous sinus involvement is suspected.

ORAL ANTIBIOTICS ARE NOW THE PRIMARY TREATMENT OF CHOICE FOR INFECTIVE ORBITAL CELLULITIS: YES
R. Guthoff, K. Manousaridis
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Orbital cellulitis is a serious condition which requires urgent treatment in order to avoid sight or life threatening complications. Careful clinical assessment and implementation of radiological examinations is of great importance for defining the stage of disease and detecting possible intracranial extension. Patient age and presence of factors implying high risk of complications such as sinus frontalis infection, dental origin of infection, air in the orbit, and evidence of chronic sinusitis should be taken into account for decision making regarding treatment. Many patients present with early disease, which carries a low risk of serious complications in the modern antibiotic era. Although according to almost all publications to date intravenous antibiotics will be required to manage orbital cellulitis an extensive review of the literature failed to provide definite answer to the question if intravenous antibiotics are superior to oral antibiotics in the management of this condition. Many antibiotics, such as those of the quinolone drug class, whose oral form is practically bioequivalent to the intravenous form, are available for the management of the most likely causes, such as Pseudomonas aeruginosa. Studies comparing the oral with the intravenous administration of the same or other antibiotics showed similar effects in the pharmacokinetics and management of infections. Moreover through oral administration complications associated with venous catheterization are avoided and the costs of therapy are considerably reduced. Subsequently oral antibiotics can be considered the primary treatment of choice for infective orbital cellulitis especially in cases of early disease (Stage I. or II. according to Chan’s classification) or in cases where factors implying high risk of complications are absent.

IOP FLUCTUATION: NOT IMPORTANT
A. Heijl
Sweden

Fluctuation of intracranial pressure is often said to be of importance for glaucoma progression. There is clear evidence that IOP level (e.g. mean IOP) is related to progression. It is also known that IOP fluctuation tends to be proportional to IOP level. Therefore, IOP fluctuation is also related to progression. The important issue, however, is whether IOP fluctuation is an independent risk factor or not, i.e. is IOP fluctuation an extra risk factor once means IOP has already been taken into account? There are studies claiming that this is the case, but most of them have serious design errors. The most solid studies indicate that IOP fluctuation is not an independent risk factor. Thus, the clinician should take IOP level into account, but does not have to spend time registering fluctuations, nor to consider them in clinical decision-making.

PRE-PERIMETRIC GLAUCOMA: DON’T TREAT
A. Heijl
Sweden

Sometimes careful clinical examinations seem to show that a patient has glaucoma, despite the fact that the results of proper visual field testing are entirely normal. Should such patients be treated? The answer is almost always no, and here are some reasons why:

1. Pre-perimetric glaucoma is a difficult diagnosis and is rather likely to be erroneous. Normal eyes with large discs are, e.g., often erroneously judged to be glaucomatous. The risk for such faulty classification is even larger in patients with suspect glaucoma, e.g. patient with elevated IOP or a positive family history of glaucoma.
2. The goal of glaucoma treatment is to prevent loss of Quality of Life. QoL is not reduced until considerable field loss has been encountered. Most patients with pre-perimetric glaucoma will never suffer any loss of QoL even if they develop visual field damage.
3. Receiving a diagnosis of glaucoma reduces a patient’s QoL.

SELECTIVE PERIMETRY IS OFTEN USEFUL: NO
A. Heijl
Sweden

Selective perimetry was developed with the hope that such techniques would be able to identify glaucomatous visual field loss (GVFL) at an earlier stage than what is possible with
standard automated perimetry (SAP). The idea that stimulating a subset of retinal ganglion cells would diminish the redundancy was an attractive one, and several approaches were made including short-wave automated perimetry (SWAP) with blue stimuli on a yellow background and the frequency doubling technique (FDT). Several early studies seemed to support the value of the new techniques.

Later well designed and also longitudinal studies on SWAP have shown, however, that this technique does not detect GVFL earlier than SAP. At the same time serious design flaws have become apparent in the early studies that were often quoted as supporting selective perimeter. SWAP also has disadvantages as compared to SAP in glaucoma management: much larger test–rest variability, higher sensitivity to media opacities and reduced dynamic range. There is, therefore, no reason to use SWAP in glaucoma care today. Evidence is also lacking for other selective perimeter modalities. The ophthalmologist, therefore, can rely on SAP alone, thus benefiting from the good interpretation tools that are available for SAP, both for diagnosis and for follow-up.

**OCULAR MUCOUS MEMBRANE PEMPHIGOID: INITIAL TREATMENT SHOULD BE CYCLOPHOSPHAMIDE**

D. Jabs

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Ocular mucous membrane pemphigoid (MMP) is an autoimmune disease characterized by a cicatrizating conjunctivitis and deposition of immunoreactants at the basement zone of epithelial structures of mucous membranes. It is a systemic disease; ~80% of patients with ocular MMP will have involvement of other mucous membranes, most often the oropharynx. Diagnosis requires immunohistologic confirmation on biopsy, as there are other causes for cicatrizating conjunctivitis. Untreated ocular MMP results in conjunctival scarring and shrinkage, trichiasis, ocular surface damage, and corneal blindness. Control of ocular inflammation is key in preventing further conjunctival scarring and ocular surface damage. Treatment options include: Dapsone, prednisone and cyclophosphamide, and prednisone and other immunosuppressive agents (e.g. azathioprine, mycophenolate, etc.). In a series of 94 patients with ocular MMP (Ophthalmology 2008;115:2146), control of ocular inflammation was achieved in 83% of patients by 1 year of treatment. Treatment with prednisone generally is discontinued within 6 months, and the total course of cyclophosphamide is ~18 months. A remission (defined as inactive disease for >3 months after discontinuation of therapy) was achieved in 91% of patients with a regimen of cyclophosphamide and prednisone v 67% of patients treated with other regimens (P=0.03). Relapse rates after achieving a remission were 0.03/person-year (PY) for the cyclophosphamide regimen v 0.23/PY for other regimens (P=0.006). These data demonstrate that a regimen consisting of prednisone and cyclophosphamide is superior to other regimens in inducing a remission and preventing subsequent relapse. Side effects (leukopenia, hematuria) generally were reversible, but discontinuation of cyclophosphamide therapy for side effects occurred at the rate of 0.20/PY; nevertheless 74% of these patients achieved a remission. Long-term studies have demonstrated no adverse effects on lifespan from cyclophosphamide therapy. (Br J Ophthalmol 2009;89:2480), demonstrating its safety if used judiciously.

**SCREENING FOR GLAUCOMA: NOT JUSTIFIED**

H. Jampel

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I would love to be able to tell you that we currently have the tools to screen for glaucoma, and that widespread screening for glaucoma would result in a decrease in loss of vision as well as improved quality of life for individuals with as yet undiagnosed glaucoma. However, I cannot. No one has studied the pros and cons of screening for open angle glaucoma more cogently than the United States Preventive Services Task Force and their chairperson, Ned Calonge, and therefore I will summarize the Task Force’s arguments for you.

The Task Force report reminds us of the potential harms of screening for a disease, which include the false positives that result in patient anxiety, as well as the cost and inconvenience of additional testing, and the false negatives, which give a person a false sense of security. In addition, a screening test may detect a true case of disease, but maybe it occurs in an individual who never would have become symptomatic from the disease. Finally, unless early detection can be demonstrated to be beneficial to individuals, screening and treatment steals resources from other diseases. Finally, the screening itself may be harmful, but that argument has little relevance to glaucoma. The ultimate rationale for performing screening for open angle glaucoma would be that screening leads to a decrease in the visual impairment and loss of quality of life in our societies. The task force was not convinced that this rationale is sufficiently supported by existing data. In their analytical framework, screening would lead to the detection of asymptomatic cases of glaucoma, in whom treatment would be started which would reduce the number of individuals who become visually impaired. The harm done to individuals through screening and treatment would also have to be less than the benefit gained from reducing visual impairment from glaucoma.

The Task Force’s take on the pathway from screening to reduced visual impairment is as follows:

1. There are good screening tests to detect elevated intraocular pressure and open angle glaucoma.
2. There is good evidence that lowering IOP reduces the incidence of asymptomatic visual field loss, but no evidence that this translates into less visual impairment.
3. There is good evidence that lowering IOP in eyes with early asymptomatic visual field loss reduces progression of visual field loss, but no evidence that this translates into less visual impairment.
4. There is good evidence that treatment of glaucoma can result in harm.

Therefore, the main missing link in proving the usefulness of screening for glaucoma is the lack of evidence that preventing initial visual field loss or preventing the progression of early visual field defects reduces severe visual field loss and visual impairment. For this reason the Task Force has continued to give glaucoma screening an “I” or “insufficient evidence” rating.

Is the story different for closed angle glaucoma? One of our course faculty, Paul Foster, has been instrumental in studies of angle closure throughout Asia. He and his colleagues recently published a study in the British Journal of Ophthalmology entitled “Randomised controlled trial of prophylactic treatment to prevent primary angle closure glaucoma.” They randomized a Mongolian population to receive or not receive an ultrasound examination of anterior chamber depth. Those subjects in the screened group who had an anterior chamber depth of less than 2.53 mm underwent a comprehensive eye exam and received a laser PI if the angle was closed. Of those individuals who had angle closure, half were randomized to laser iridotomy and half were not. Six years later individuals in the observation group, and individuals in the screening plus laser iridotomy group were examined. There was no difference in the incidence of angle closure glaucoma between the two groups.

I hope that future research will eventually convince third parties that glaucoma screening is worthwhile. If we can prove that it can prevent important visual loss we will still have to grapple with the cost of such screening and treatment, and the issue of cost-effectiveness.

References:

 Articles published in medical journals are an important source of the information that clinicians use in making decisions about patient care and that researchers use in planning their next experiment. Therefore, if it is an editor’s obligation to insure that the most important articles are published and that those that are published have as little bias as possible. For the past eight years, as Associate Editor-in-Chief of Ophthalmology, the journal of the American Academy of Ophthalmology, I have grappled with these issues for almost all editorial decisions involving glaucoma manuscripts.

Bias exist in both the generation of the manuscript by the authors and in the evaluation of the manuscript by the reviewers and editor. The sources of this latter bias is the subject of this talk.

An editor is subject to many of the same intellectual and financial biases as authors and reviewers. For a clinical journal such as Ophthalmology, the editor must decide whether an article has enough “clinical relevance” to merit publication. Apart from an opinion about where on the spectrum of clinical relevance a submission needs to be, the editor also brings prejudice to the particular subject matter. For example, he/she might feel that retina is more important than pediatric ophthalmology. Furthermore there may be prejudices against a particular discipline in clinical science, such as economic analysis, on life studies. These intellectual biases are difficult to monitor although a vigilant editorial board may help to reduce them.

Financial conflicts are easier to detect than intellectual. Clearly if the editor has the potential to gain financially from the publication of an article reporting favorable results on a drug or technology there is a conflict. The same holds for publication of negative results on a competing technology. Ownership of equity or stock in a company by the editor or a family member, or participation on an advisory board or speakers bureau are clearly conflicts. However, there may be much more subtle interactions that are harder to discern.

There are several approaches to financial conflicts. Disclosure of the conflicts is the simplest step but may do little to reduce the effect of the conflict. Management of the conflict may involve placing stocks in escrow, or having a third party advise on the appropriateness of the financial relationship. The most definitive solution to financial conflicts would be to ask all reviewers, editorial board members, and editors to divest themselves from all financial interests related to ophthalmology and eye research. This is difficult to request of volunteers who are already giving of their time without compensation. In an ideal world editors and/or editorial board members would be compensated in exchange for divesting of financial interests, but this would likely be prohibitively expensive.

### INITIAL SURGERY FOR GLAUCOMA SHOULD A TRABECULECTOMY

H. Jampel

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A couple of decades ago, the only option considered for the first surgical approach to lowering intraocular pressure (IOP) was a trabeculectomy. However, over the past two decades, numerous techniques have been developed to challenge the primary role of the trabeculectomy. Despite the significant strides that alternative surgical procedures have made, I will argue that trabeculectomy still reigns as king when it comes to the initial surgery treatment of glaucoma. Let’s discuss the other procedures that might displace trabeculectomy, starting with cataract surgery. Cataract surgery by phacoemulsification has been shown to lower IOP. However, the effect in eyes without terribly high IOP to begin with is small, does not begin to approach the mean 40% IOP reduction that we can expect, or trabeculectomy, and will rarely deliver the IOP in the low teens or even lower that many surgeons desire for their glaucoma patients. For patients with bona fide glaucoma with visual field loss, cataract surgery alone is not the best option for lowering IOP.

Trabeculectomy, canaloplasty, and endolaser cyclophotocoagulation of the ciliary processes are recent techniques that can lower IOP without producing a filtration bleb, the Achilles’ heel of trabeculectomy. Trabeculectomy removes trabecular meshwork and inner wall of Schlemm’s canal from an ab interno approach. It does not “spend” conjunctiva that may be necessary for future glaucoma surgery and can be done in an eye with pseudoexfoliation, but it does not often result in IOP below the midteens and is not appropriate for eyes needing lower IOP. Canaloplasty, like trabeculectomy, does not produce a bleb, but does require extensive conjunctival and sclera surgery, reducing the options available for future surgery, and like trabeculectomy, will not produce really low IOP. Endolaser cyclophotocoagulation is not possible in phakic eyes, and the general bias in the glaucoma community against procedures that damage the ciliary processes currently preclude its consideration as a primary surgery.

The Express mini shunt has been portrayed as an alternative to trabeculectomy, but is really just a variation on trabeculectomy. One is still creating a hole in the eye wall covered by a partial thickness scleral flap, and the formation of a bleb is an integral part of the operation. The Express mini shunt variant of the trabeculectomy does eliminate the need to excise a small piece of the eye wall and the need to perform a iridectomy, but at the price of introducing a metallic foreign body into the eye. The rationale for implanting the Express mini shunt must be either greater effectiveness in lowering IOP, or greater safety. In one small, single surgeon, randomized controlled trial in the Netherlands, de Jonge reported greater effectiveness with the Express mini shunt compared to trabeculectomy, and a similar complication rate. The success rate for trabeculectomy, however, was unusually low in that study. Maris et al. reported the Express mini shunt compared to trabeculectomy and found similar success rates, but the Express eyes had a lower incidence of early postoperative hypotony.

Aqueous drainage device surgery certainly merits legitimate consideration as an initial incisional surgery for glaucoma. Following on the heels of the Tube vs. Trabeculectomy study, the Primary Tube vs. Trabeculectomy (PTTV) study is now underway to answer precisely the question being addressed in this debate, i.e. which is the better primary operation, tube or trabeculectomy? I argue that until we have the results of the PTTV study, we should continue to regard trabeculectomy as our initial surgical approach for most types of glaucoma. My reservations about aqueous drainage device (ADD) surgery as initial surgery are fourfold. First, although the TVT results are encouraging, in a study with much longer follow-up than the TVT, Stein et al. have reported more serious complications, such as endophthalmitis and retinal detachment, after ADD surgery than after trabeculectomy. Second, there are unresolved concerns about the long-term effect of ADD tubes upon the cornea. Third, the need for a patch graft over the tube introduces a second foreign body onto the surface on the eye with the possibility of further complications. Lastly, the use of suture release techniques in trabeculectomy and post-operative use of antifibrosis agents gives the surgeon the power to modify a trabeculectomy after surgery, an opportunity not usually possible with ADD surgery.

I share the hope of my colleagues that the procedures that I have mentioned will eventually displace trabeculectomy as the best choice for initial surgery. However, with the current state of the art it still the trabeculectomy, even with all its warts, that has the best risk/benefit ratio. For that reason, I encourage those of you in the audience who perform glaucoma surgery to continue to regard trabeculectomy as your initial choice.

References


We know that the level of IOP is associated with the likelihood that an eye has glaucomatous optic nerve damage. We also know that when the IOP is elevated in experimental animals, and when there is a case of a unilateral marked elevation of IOP in humans, such as traumatic glaucoma, that glaucomatous optic nerve damage occurs, proving that elevation of IOP can cause glaucomatous damage. We have also demonstrated that lowering of IOP reduces the incidence of glaucoma in ocular hypertensives (Ocular Hypertension Treatment Study) and that lowering the IOP slows the progression of glaucoma in eyes with early glaucoma (Early Manifest Glaucoma Trial).

The level of IOP is constantly in flux. It has been postulated that fluctuation in IOP could be bad for the optic nerve, with a presumed mechanism of subjecting the ganglion cell axons to increased mechanical stress due to movement of the lamina cribrosa or by compromising blood flow and nutrition to the optic nerve. Therefore investigators have studied whether fluctuation in IOP is associated with optic nerve damage. We have long recognized that in the office some eyes seem to have close to the same IOP from visit to visit, whereas others have IOP that seems to differ, sometimes high, sometimes low. This variation has been referred to as long-term fluctuation, and has been addressed in the context of some of our best randomized clinical trials. In these studies, the variance of IOP measurements taken every six months is studied in relationship to the likelihood of progressive glaucoma damage. However, the data concerning long-term fluctuation and worsening glaucoma has generated conflicting results. No relationship was seen in the EMGT, and the relationship in the Advanced Glaucoma Intervention Study (AGIS), has now been been revised to include only those eyes with low, but not high IOPs. Hong et al. reported less glaucoma progression after combined cataract and glaucoma surgery in the eyes with the least fluctuation between visits.

Short-term fluctuation generally refers to variation in IOP throughout the day and night (circadian rhythm). Certainly it is plausible that fluctuations occurring in this time frame could be deleterious to the optic nerve. Asrani et al. reported that in patients with glaucoma with office IOP values in the normal range, short-term IOP fluctuation measured using home tonometry was a risk factor for progression. Collaer et al. reported that patients with normal-tension glaucoma showed a significant relationship between visual field deterioration and the range and peak of IOP during a single day. Critics appropriately point out that both these long-term and short-term studies only sample the IOP during an infinitesimal fraction of the time that the IOP is exerting its effect on the optic nerve, and that such investigations will remain inconclusive until we can perform continuous IOP monitoring. Preliminary work with an indwelling tonometer in monkeys performed by Claude Burgoyne and colleagues in Oregon suggests that there are wide fluctuations in IOP occurring many times a second. In the absence of definitive data, what is the clinician to do? If we had waited for definitive evidence that lowering IOP was beneficial in glaucoma, we would have done little IOP lowering before 1990 or even earlier. Fortunately we did not wait. Unlike, IOP lowering, however, which has potential side effects, attempting to reduce fluctuation carries no increased risk over IOP lowering. In attempting to reduce fluctuation, and practically speaking that means from office visit to office visit, one is reducing the IOP. I doubt that even the most fervent believers in the importance of fluctuation would argue that than an IOP that is always 21 mm Hg is safer than an IOP that is sometimes 15 mm Hg and sometimes 21 mm Hg. On the other hand, I do believe that always measuring 18 mm Hg is better than sometimes measuring 18 mm Hg and sometimes measuring 19 mm Hg, which is better than sometimes measuring 16 mm Hg and sometimes measuring 21 mm Hg. In the busy clinic, high fluctuation means that the IOP is not adequately controlled and that more aggressive IOP lowering may be warranted.
sulphapyridine, though not statistically significant. Inflammation was controlled in 70 % of patients, and this rate was also true for the severe cases treated with cyclophosphamide. The response increased form 73% in a single-agent treatment to 87% using a combination treatment composed of steroid-sulph-pha-immunosuppressive agent. Among the immunosuppressive agents, cyclophosphamide and mycophenolate achieved similar results. The step-up treatment regimen typically begins with dapsone and sulphapyridine in the mild cases, followed by methotrexate. If insufficient response occurs, treatment may be stepped up to include azathioprine, followed based on clinical evaluation by mycophenolate. A further step-up includes cyclophosphamide and when necessary also immunoglobulins. Using the “blast” approach, the severe cases are treated by the most efficient drug, while the ones who may respond to less aggressive therapy, will be exposed to this agent unecessarily. In addition, since cyclophosphamide can be used for a limited period, no longer than 18 months, the step down approach provides a gradual decrease in the intensity of immunosuppression when control is achieved.

The use of early cyclophosphamide is based on the assumption that early aggressive treatment changes the course of the disease. However, there is no clear evidence to this assumption. It may well be that the intrinsic severity of the disease course in some patients is less than others, and may be sufficiently controlled by other immunosuppressive agents. Moreover, cyclophosphamide was not compared to biologic agents that are frequently used in recent years, and accumulating data point to favorable outcome. Needless to mention the need for strict periodical clinical follow up in these patients.

So, back to our initial question: To blast or not to blast? Blast only when required.

In the absence of clear evidence, the tailored approach provides sized treatment based on the severity of the disease with the ability to adjust during the course of the disease.

THE GLOBE SHOULD BE PRESERVED
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It is common practice in some countries to enucleate/eviscerate severely injured eyes if the eye also loses its ability to perceive light (NLP). The reason given to proceed with globe removal is typically the fear of sympathetic ophthalmia (SO). In reality, while SO is indeed a postinjury complication that needs to be discussed with the patient, it is extremely rare. In the literature a rate of 1/1,500 severe injuries is given, but it is not an exact number. More telling is the fact that since World War II, only a single case has been reported in all wars combined. Furthermore, with early diagnosis and proper treatment, the sympathizing eye has a 2/3 chance of preserving reading vision (the outcome of the aforementioned case was also favorable).

If the patient is made aware of these numbers during counseling, it is unlikely that he will select eye removal, but opt instead for the trauma specialist to explore the globe surgically and make every effort to restore vision or at least normal anatomy and avoid the serious psychological trauma of enucleation/evisceration.

AVASTIN: WHAT EVIDENCE AVAILABLE
P. Lancetta, D. Veritti
Italy

Background: Neovascular age-related macular degeneration (AMD) is a leading cause of blindness, with an increasing incidence as the elderly population expands. Vascular endothelial growth factor (VEGF) plays a key role in exudative AMD pathogenesis. Bevacizumab is an anti-vascular endothelial growth factor (VEGF) monoclonal antibody that inhibits vascular permeability and endothelial cell proliferation and migration. Bevacizumab is approved for the treatment of various malignancies, including colorectal and non-small cell lung cancer, and it is administered off-label for intracocular use for choroidal neovascularization (CNV) due to age-related macular degeneration (AMD).

Aim: To provide evidence for safety and efficacy of intracocular use of bevacizumab.

Methods: A selective literature search was utilized to illustrate differences between the full-length anti-VEGF antibody (bevacizumab) and the Fab anti-VEGF antibody fragment (ranibizumab) as regarding their pharmacodynamic and pharmacokinetic properties in the intracocular environment and the different profile in inflammatory response. A systematic review was conducted to assess the safety and clinical effectiveness of intravitreal bevacizumab. The quality of included studies was assessed using standard methods. Available data from head-to-head studies comparing ranibizumab to bevacizumab will be reviewed.

Results: Evidence available from in-vitro and in-vivo studies showed that bevacizumab and ranibizumab differ in their retinal penetration capabilities, complement- or cell-mediated cytotoxicity and systemic half-life. Data available from randomized clinical trials suggest that the administration of intravitreal bevacizumab in patients with exudative AMD leads to an improvement both in visual acuity and central retinal thickness. Recent reports highlighted ocular inflammation and systemic side effects after bevacizumab ophthalmic use. Ocular adverse events reported may include corneal abrasion, photosensitivity, endophthalmitis, retinal detachment, inflammation or uveitis, cataract progression, acute vision loss, central retinal artery occlusion, subretinal haemorrhage, retinal pigment epithelium tears. Systemic adverse events include blood-pressure elevation, cerebrovascular event, transient ischaemic attack, and death. A recent paper evaluated the association between therapies for age-related macular degeneration and risks of all-cause mortality, incident myocardial infarction, bleeding, and incident stroke. The direct comparisons of ranibizumab therapy vs bevacizumab therapy showed that the hazards of mortality and stroke were significantly lower with ranibizumab therapy than with bevacizumab therapy. An update on head-to-head trials comparing intravitreal bevacizumab to ranibizumab for the treatment of CNV secondary to AMD will be provided.

Conclusions: This systematic review shows that intravitreal bevacizumab is effective in improving visual acuity in patients with exudative AMD. According to current reports severe adverse events are rare. Results from well-conducted, controlled, randomized clinical trials, with a large number of patients, are needed to assess the differences in safety profile and clinical efficacy between bevacizumab and the FDA-approved ranibizumab. Until then, differences in efficacy and safety profile between bevacizumab and ranibizumab remain controversial.

SYMPOSIUM ON THE TREATMENT OF TRAUMATIC OPTIC NEUROPATHY: STEROIDS SHOULD BE USED
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Traumatic optic neuropathy (TON) is a clinical diagnosis supported by radiographic findings. Although making the diagnosis is typically not difficult, the treatment of TON remains controversial. A prospective International Optic Nerve Trauma Study (IONTS) failed to establish a beneficial effect for surgery with optic canal decompression or medical treatment with various doses of corticosteroids. In addition, multiple flawed retrospective research studies have provided conflicting results on the efficacy and safety of corticosteroids and some animal studies have suggested beneficial effects of steroids on the injured optic nerve. Thus, neither corticosteroids nor optic canal decompression can be considered to be the standard of care for TON. In addition, in the CRASH study of head injury, compared with placebo, the risk of death from all causes within 2 weeks was higher in the group allocated to corticosteroids (1052 [21.1%] versus 893 [17.9%]) with a relative risk of 1.18 [95% CI 1.09-1.27]; p=0.0001). This relative increase in death rate due to corticosteroids did not differ by injury severity (p=0.22) or time since injury (p=0.05). In summary, the treatment decision for TON remains controversial and must be individualized to each patient circumstance. Although the old adage “cant hurt, might help” might still be
Acute retinal necrosis (ARN) is a necrotising retinitis most commonly caused by herpes zoster (HZV) or herpes simplex (HSV types 1 and 2) virus. It usually starts in the retinal periphery and is commonly associated with an anterior uveitis. It can be unilateral or bilateral at presentation or progress from unilateral to bilateral disease. Vision loss is common. Patients may be immunocompetent or immunocompromised and of all ages.

Treatment is with anti-viral drugs and until recently intravenous aciclovir has been the only available option as oral aciclovir does not achieve an MIC within the eye. The dose given is 5-10mg/kg tds (usually 10mg/kg tds as this is the required dose for HZV) and therefore requires the patient to be hospitalised. The intravenous treatment is given for 7-14 days and is usually followed by a prolonged course of oral aciclovir 800mg x 3/day. Some ophthalmologists give intravitreal foscarnet at presentation and some do barrier laser to surround the involved area and reduce the risk of posterior pole retinal detachment. Oral steroids, topical steroids and mydriatics together with treatment for raised intraocular pressure if present may also be required.

More recently valaciclovir has come into clinical use. It is a prodrug for aciclovir and is given orally. At 2g tds it achieves the same blood levels as when aciclovir is given at 10mg/kg tds intravenously and therefore has multiple advantages in that the patient does not need to be hospitalised nor have an intravenous line. Adequate intracocular penetration has been demonstrated using vitrectomy samples. Several small studies have confirmed that valaciclovir is effective in the management of ARN and investigators have used oral doses of 1g tds or 2 g tds for 6 weeks+. Oral famciclovir has also been successfully used in the management of patients with ARN. The side effects of the oral drugs are minimal and dose reduction is required in patients with renal compromise.

This paper will present the available data on ocular outcomes using intravenous aciclovir and the oral drugs and will demonstrate that oral valaciclovir is a safe and effective alternative. The best dose is still unclear but both 1 and 2 g tds are effective in the groups of patients studied.

**ROLE OF AUTOFLUORESCENCE FOR MONITORING PROGRESSION OF GEOGRAPHIC ATROPHY IN AMD: PRO**

E. Midena

**Italy**

Geographic atrophy (GA) is the advanced atrophic form of age-related macular degeneration that increases in prevalence with age and results in progressive moderate and severe visual loss over time. GA is characterized by the development and progressive enlargement of areas of retinal atrophy that extend through the outer neuroretina, retinal pigment epithelium and choroid, effectively depriving affected areas of light sensitivity. GA is commonly monitored by fundus photography, but this technique suffers some major intrinsic limitations, mainly related to moderate/poor reproducibility. Recently, optical coherence tomography (OCT), namely spectral-domain OCT, has been used to study the pathophysiology of geographic atrophy. But fundus autofluorescence (FAF) may be now considered the most consistent diagnostic method to quantify and follow the evolution of GA. FAF is based on the normal autofluorescence properties of the retina, mainly RPE. Development and progression of GA are characterized by reduced FAF, with increasing FAF signal in the areas bordering the purely atrophic lesions. FAF is currently visualized in vivo with non invasive techniques, and some instruments allow to detect both short-wavelength and near-infrared autofluorescence. Estimates of lesion growth obtained using FAF are in agreement with natural history data, and provide a reliable method to adequately follow GA. The high contrast difference between atrophic and non-atrophic retina allows for accurate delineation of lesion boundaries, and quantification of uni- or multi-focal atrophic areas on FAF images using customized image analysis softwares. This allows for noninvasive (automatic) monitoring of the progression of atrophy over time and therefore the assessment of the beneficial effect of any novel agent aiming at slowing GA progression. The previously mentioned specific pattern around the atrophic areas may also represent a new marker to distinguish different progression phenotypes.

**DOES SILICONE OIL STILL HAVE A ROLE IN COMPLICATED RD WITH PVR?**

**SILICONE OIL IS THE KEY TO SUCCESS IN THESE DIFFICULT CASES**

W. Mieler

**Chicago, IL, USA**

The debate regarding the use of tamponade agents in the setting of a retinal detachment (RD) with proliferative vitreoretinopathy (PVR) has been ongoing for the past 25 years. The choice of tamponade agent ranges primarily between long-acting intraocular gases (SF6 and/or C3F8) versus silicone oil, though more recently heavy silicone oil and the use of postoperative perfluorocarbon (PFC) liquids have entered into the discussion as well. In the mid-1980s, in an attempt to address this issue, the Silicone Oil Study provided a number of comparative studies, assessing the use of SF6 or C3F8 versus silicone oil. The study clearly showed that silicone oil and/or C3F8 provided superior outcomes in comparison to SF6. Regarding the comparison between C3F8 and silicone oil however, the final visual acuities were comparable, along with reoperation rates, and the rate of corneal keratopathy. The study did show a lesserened rate of hypotony with silicone oil, in comparison to the use of C3F8.

While the principle outcomes reported by the Silicone Oil study generally hold true today, subsequent studies (Quiram 2006) have suggested that silicone oil may actually provide better long-term visual and anatomic outcomes. Additionally, in the setting of open-globe injuries with RD and PVR, there is a marked tendency to utilize silicone oil, as there is oftentimes a much greater need for retinotomies and retinectomies. Silicone oil provides a more extended tamponade for these types of problems, especially when there is trauma involving the inferior aspect of the retina.

Silicone oil does provide a number of advantages in comparison to long-acting intraocular gases. It provides a prolonged period of tamponade (until the silicone oil is removed), patients can see through it, there are no restrictions on air travel, it allows a better chance of achieving at least a partial retinal attachment, and as indicated above, there is a lesserened rate of postoperative hypotony. Disadvantages include the fact that it does not prevent reproliferation (nor does any other agent), emulsification may occur, it alters the refractive state, there is concern regarding cataract formation and corneal toxicity, there is a significant chance of transient elevated IOP, and of course there is the need for a second surgery to remove the silicone.

As was noted at the start of this abstract, heavy silicone oils (Sandner 2007, Regler 2009, Er 2010, Li 2010, Rizzo 2010) and the use of postoperative liquid PFCs (Drury 2010) may also play a role in the management of complex RDs with PVR, though there is not enough data at the present time, to fully define their respective roles.

Overall, anatomic stability can be achieved in approximately 85 to 90% of cases, with functional success (VA > 5/200) in about 75% of cases.

I believe that the current literature supports the use of silicone oil in many of these complex RDs with PVR, and this holds especially true in the setting of open-globe injuries. While at the present time, successful repair of complex RDs involves primarily a meticulous surgical approach (Aaebeg 2011), the choice and use of the long-term tamponade agent may make a difference. Of course, we all will welcome the time when pharmacologic adjuncts (inhibitors of cellular proliferation,
Idiopathic epiretinal membrane (ERM) is a common condition that may cause various degrees of visual disturbances, mainly blurred vision and distortion. The only existing treatment is vitrectomy with membrane peeling, but despite decades of experience with ERMs there are no universally acceptable criteria for recommending surgery or definitive guidelines for the surgical techniques. There were many recent advances in vitreoretinal surgery that made vitrectomy for ERM a very safe and effective procedure, particularly small gauge instruments and vital dyes that stain the ERM and the ILM and greatly facilitate their removal. The rapidly developing OCT technologies offer an excellent imaging modality for evaluating the pre- and post-operative status of the retina, the ERM and the vitreous, and are an indispensable tool in the management of this condition.

The prognosis for improving vision after vitrectomy depends mainly on the initial visual acuity, the duration of the ERM, the structure of the macula on OCT, and the surgical technique. Eyes with long-standing ERM and lower visual acuity are less likely to improve than eyes with recent ERM and relatively good VA. The risks associated with the surgery are few, and include mostly treatable conditions such as cataract and retinal detachment. Moreover, the natural history of untreated ERM is often associated with slow but progressive decline in visual acuity, and after several years of observation many of these eyes have VA far below reading or driving ability. Taken together, the available information on the efficacy and safety of vitrectomy for idiopathic ERM leads to the inevitable conclusion that vitrectomy should be performed relatively early in the course of the ERM, in order to achieve good anatomical preservation of the macula and excellent visual results. Yes, we should perform ERM peeling in eyes with good visual acuity.

Question:
A 65 years old physician presents with a history of progressive deterioration of vision in his left eye for 6 months, with blurring and distortion. His visual acuity is 20/40, and there is an ERM, with homogeneous thickening, preservation of the outer layers of the retina and foveal thickness of 420 microns. This is the better eye, as the right eye had CRVO and the VA is 20/400. The best management of this case is:
1. Observation, and if his vision drops to 20/80 perform vitrectomy
2. Perform in the near future a vitrectomy with ERM peeling, and in most cases also ILM peeling
3. Intravitreal injection of anti-VEGF to reduce the edema and if this fails – try intravitreal triamcinolone
4. This eye should not be operated at all, as it is the good eye, and the risks from surgery are too great compared with the relatively good natural history of the disease.

TRAUMATIC MACULAR HOLE
J. Moisseiev
Israel

Traumatic macular holes usually occur following blunt ocular trauma, but other causes have also been reported, including accidental laser injuries, lightning and electrical shock. The pathogenesis in blunt trauma was not definitely established, but it is possible that the acute compression-decompression force exerted on the globe may cause local posterior vitreous detachment, leading to dehiscence in the fovea or to avulsion of a small operculum. These holes usually develop shortly after the blunt trauma, and are often located within an area of pigment changes induced by the associated traumatic edema in the posterior pole. In laser injury the macular hole results from coagulation necrosis following the intense laser burn, and the hole can develop in the days or weeks following the injury. The surgical management of traumatic macular hole is similar to that of idiopathic macular holes, and includes vitrectomy, ILM peeling, and fluid-gas exchange. As many of these patients are young it is often necessary to perform a mechanical removal of the posterior cortical vitreous. Selection of cases and timing of surgery are important, and the anatomical and functional outcomes often depend on associated trauma-related ocular pathologies. In following these patients it is important to remember that spontaneous closure of the hole can occur but is not common, and surgery should not be deferred for too long, as long standing holes are associated with poor prognosis.

Question:
A 27 years old mail sustained a football trauma to his right eye. Two days later a macular hole was observed (and documented
Rhegmatogenous Retinal Detachment (RD) is the most common type of retinal detachment and affects up to 18 per 100,000 people per year. I would be the first to agree that when PR works, it works extremely well and the surgeon should always consider it as a treatment option. However, it is extremely dependent upon excellent patient selection, surgical experience and very specific case criteria.

When considering the treatment options for RD the surgeon has to take into consideration many factors, including his own level of experience, particularly with regard to cryopexy so that this is not over-applied as this may lead to PVR. Prior to operating, the surgeon must have sufficient time to have carried out a detailed examination of the retina. Postoperative examinations are also vital to successful resolution of RD and the surgeon needs to be available to re-operate immediately if the procedure has not been successful. Further criteria that have to be taken into account is the patient’s ability to physically and mentally cope with the required post-operative posturing and their commitment to the necessary follow-up examinations. They should also be advised that they will be unable to fly for one week after the operation. Patients should not be offered PR if their fellow eye had a giant tear, unsuccessful PR treatment previously or where there are difficulties in examining the retina e.g. cataract, capsular clouding, vitreous hemorrhage or small pupil.

Published results of single operation success rates for cases treated using PR are much lower than those for cases treated with PPV or buckling. Survey figures for single operation success rates were published as 75.5% for PR, 85% for PPV and 88% for buckling. Another report shows an average primary attachment rate of 91% when treating 1462 detachments with Minimal segmental bucking without drainage. The lower initial success rates for PR may be due to reopening of the original break and/or new/missed breaks; both SB and PPV provide additional examination opportunities during the procedures. PR success rates are negatively influenced by pseudophakia, aphakia, a large number of retinal tears and a large area of detached retina. Day et al. published data from a database spanning 17 years with 1 year of follow-up which showed that the rate of second retinal detachment operations for patients who had undergone PR were much higher (40.6%) than for those who had scleral buckle performed (19%). After controlling for demographic variables and ocular comorbidities PR patients were stated as being 3 times more likely to require second operations than scleral buckle patients. There was no significant difference between scleral buckle patients and those who had PPV performed with regard to second operation rates. Whilst scleral buckle is seen by many to be the ‘gold standard’ for RD repair, PPV is also said to have many advantages over PR. These include elimination of vitreous traction and removal of the vitreous as a stimulant for PVR and, importantly, an improved internal search for retinal breaks.

Prone positioning (‘face down positioning’, ‘posturing’) of at least 5 days is cited for hole closure. The majority of authors in the last 10 years use 5 days or more prone positioning. This paper will discuss the mechanism of macular hole closure with SD OCT. It must be emphasized that the hole closure begins at the inner surface of the retina. Sclerotomy by ILM peeling allows glial cells to proliferate. Literature suggests that a scaffold or template is needed for glial cells to migrate along and this can be provided by the interface between the endotamponade agent and the retina. It seems logical therefore that a longer lasting or more thorough tamponade would produce the required results.

We must distinguish prone position from tamponade effect as both have their roles to play in MH closure. Authors have argued that an air/gas tamponade ‘bubble’ produces a ‘waterproofing’ effect, preventing the newly formed post-vitrectomy aqueous humor from contacting the macular and interfering with the bridging of the MH. Furthermore it has been suggested that an air/gas bubble may apply a directional force to the macula producing a mechanical effect against any tractional vectors and holding the MH edges against the RPE. This is perhaps a reason why air/gas tamponades are more successful than silicone oil as SO is less buoyant and conforms poorly to the foveal depression as it makes a smaller angle of contact with the retina.

Some authors use gas/air mixture to fill the eye and which remains in the eye much longer and produces a longer lasting tamponade effect even without prone positioning. We can produce another tamponade-like effect as we presented recently with the Inverted ILM Flap Technique we do however, still need prone positioning to keep the flap in place. An SD OCT study of Eckardt showed that the majority of MH closed in the first 24-48 hours. (Not all eyes could be examined at these times.) However, some closed late and the number of patients was relatively small (33). Eckardt also points out that the follow-up time was too short to say whether late re-opening of successfully closed holes can be associated with short-term tamponading. Thus we might also question the use of short-term prone positioning in these cases. It has been shown in literature that the majority of 1-day posturing cases seem to lead to simple type closure. Should we not reflect upon the facts that for a surgeon, the anatomical aim of MH surgery is to close the macular hole and that successful small MH closures are reported as occurring on day 1. The patient however, may be equally, if not more delighted, by a post-operative improvement in visual acuity. Macular recovery may take much longer (up to one year) and longer term prone positioning may assist with the patients’ future macular recovery and VA improvement.

I believe we should also consider the fact that in the modern era, patients and relatives have a greater tendency than ever before to investigate matters for themselves. To that end, if we ‘Google’ Macular Hole Surgery the first pages of results all seem to advocate face down positioning. I am not a social scientist. However, I feel that many patients will assume a ‘better safe than sorry’ attitude and follow this Internet advice regardless of any suggestion from their doctors that prone positioning is not necessary and this may have a hidden impact on non-prone position MH closure rate figures as it is unlikely that they would report to their surgeon that they followed other advice.

**OSSN - HOW TO TREAT? TOPICAL CHEMOTHERAPY AS PRIMARY TREATMENT**

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Ocular surface squamous neoplasia (OSSN) is one of the currently-used terms for precancerous and cancerous epithelial lesions of the conjunctiva and cornea. It includes dysplasia, carcinoma-in-situ (CIN), and squamous cell carcinoma (SCC). When discussing treatment options, especially topical chemotherapy, we should clearly distinguish between in-situ squamous lesions (CIN) and invasive squamous lesions (SCC). The traditional methods of treating OSSN are surgical excision with or without cryotherapy, and some experts use...
brachytherapy. Because of the possible complications of surgical excision, cryotherapy and brachytherapy, in the early 1990’s the use of topical chemotheraphy was initiated. The first drug that was used was Mitomycin C in concentrations of 0.02% to 0.04%, with a very high response rate of about 95% and side effects that are usually temporary. Because of the superficial effect of Mitomycin C drops, it is not recommended to use them as primary treatment in invasive SCC. Other groups have used topical 5-fluorouracil (5-FU) 1% drops with very good response and with no long-term side effects. Other groups have used recombinant interferon-alpha2b in treating CIN, either via intraluminal injections or via drops, with complete clinical resolution of the tumor.

DOES SILICONE OIL STILL HAVE A ROLE IN COMPLICATED RD WITH PVR - CON: SILICONE OIL IS NOT NECESSARY AND GAS IS AS EFFECTIVE AS SILICONE

S. Rizzo
Italy

The Silicone Study was a multicentered, randomized surgical trial designed to compare the tamponade effectiveness of silicone oil versus long-acting gas in the treatment of proliferative vitreoretinopathy (PVR) by vitrectomy and associated techniques. In 1997 The Silicone Study showed that silicone oil and perfluoropropane gas were equal in most respects for the management of retinal detachments with PVR. Since then the development of surgical techniques, technology and equipment has changed the vision of the problem. In Europe Silicone oil has been the most frequently used long-term retinal tamponade during vitreous surgery for complicated retinal detachments. Even if it allowed to reattach most detached retinas, the visual outcome of the silicone oil procedure may be disappointing, due to the well known complications of silicone oil (i.e. cataract, glaucoma, corneal opacification), moreover the necessity to remove the silicone oil in a second surgical procedure can involve a risk of redetachment. The alternative method for internal retinal tamponade is the use of gases that are afflicted with much less complications. We retrospectively reviewed the charts of our patients, operated on for retinal detachment in the last 18 months, in order to analyse the anatomical and functional results with silicone oil versus gas tamponade. Regarding the last 530 consecutive surgical procedures for retinal detachment (482 eyes), silicone oil has been used in 5%, unexpansive air-gas mixture in 35%, heavy silicone oil in 1% and air in 59%. The silicone oil procedure was restricted to the most advanced cases of PVR which required relaxing retinectomy. The anatomic success rate with silicone was 72%, with gas tamponade 92%. Visual acuity of 0.05 and better achieved 21% of the eyes treated with silicone oil versus 65% of the eyes with gas tamponade. These results confirm the findings of the literature: despite of the high anatomic success rate with silicone oil, the functional results are poor. Because many complicated cases of retinal detachment can now be treated successfully with gas tamponade, currently silicone oil should remain the last step in retinal detachment surgery.

Sympathetic Ophthalmia is rare but is still encountered in clinics dealing with and specializing in Ocular Trauma. Enucleation of a traumatized eyeball, performed in proper time, has the potential of eliminating the risk of Sympathetic Ophthalmia which is a sight threatening disease of the only good eye. As far as cosmesis is concerned, in enucleation the intrascleral implant is, in most cases, smaller than the eviscerated globe. Hence, there is greater tendency of developing Enophthalmos after enucleation in comparison to enucleation. Enucleation enables us to choose a proper implant for the case, and its size is not limited to the size of the scleral cavity. All these argumental points shift the balance of enucleation versus evisceration in favor of enucleation.

SURGICAL OPTIONS FOR RECONSTRUCTION AFTER TRAUMATIC CATARACT REPAIR

D. Sachs
Israel

Traumatic cataracts occur in both open and closed globe injury, and are often accompanied by severe damage to other structures of the anterior segment. Usually, the ultimate principle and primary goal in these cases is the closure of the sustained wounds and the anatomical reconstruction and optical rehabilitation are postponed to a later date. Late scarring may modify the anatomy and proper function intensifying the need to a meticulous anatomical restoration in order to minimize these complications and enhance the visual prognosis. This presentation will focus on several surgical techniques that address the many forms of trauma related damages to the iris-lens complex. These techniques include pupilloplasty, cataract extraction in cases of subluxated crystalline lens, the use of ECTR for capsular fixation, implantation of Artisan lenses in eyes with traumatic mydriasis and lacerated iris, management of iris dialysis, management of lens and vitreous remnants, and other procedures. There are approved reconstruction techniques patterns based on expert knowledge and experience but there is enough room for personal improvisation. Careful consideration of the particular problems presented by these eyes, and the judicious selection of the appropriate reconstructive approach significantly enhances their visual prognosis.

IS SD-OCT NECESSARY AND SUFFICIENT TO GUIDE CLINICAL DECISIONS IN NEOVASCULAR AMD OR DIABETIC MACULAR EDEMA? YES

U. Schmidt-Erfurth
Austria

Neovascular age-related macular degeneration (AMD) is a frequent diagnosis in clinical routine. Diabetic macular edema (DME) is a frequent complication in the course of diabetic retinopathy causing severe vision impairment. It is characterized by focal or generalized retinal thickening due to fluid accumulation in the presence of leaking microaneurysms or generalized capillary leakage. It frequently induces formation of hard exudates and has a poor long-term prognosis. The etiology of AMD as well as DME is complex and not completely understood, but several mechanisms leading to an impairment of the blood retinal barrier and a subsequently increased fluid discharge into retinal tissue could be identified in recent years. Optical coherence tomography (OCT) has become an important tool over the last decade in the diagnosis of AMD and DME because the retinal morphology can be evaluated in detail similarly to in vivo histology. Advances in OCT technology provide novel insight into in vivo changes that occur in the human retina secondary to disease or treatment, such as retinal cysts, lipid exudates, subretinal fluid or diffuse edema. The fourth-generation OCT, SD-OCT, uses a fast spectral domain technique and performs scans in a raster pattern throughout the entire macular area at a resolution of 5um in the axial and 20um in the transverse direction. This fourth-generation system can
also be combined with an eye tracking system allowing the observation of morphological changes at the exact same retinal location over time. The fifth-generation OCT, the polarization sensitive OCT (PS-OCT), enables to detect retinal tissue due to its different qualities of polarization and allows specifically the detection of microexudates. Microexudates are precursors or parts of hard exudates typically seen in diabetic macular edema but also in AMD. Previously, we could show that these sub-clinical signs of lipid and/or lipo-protein exudation can be detected in spectral domain OCT and in polarization sensitive OCT due to their polarization changing properties. These findings give a new insight into patho-morphology and patho-physiology of DME even if hard exudates are not yet present. In AMD SD-OCT has become a crucial tool during follow-up. In early diagnostic follow-up a clear correlation is seen between morphology and function. During therapy of DME, OCT offers new information about the therapeutical mechanisms. The exact intra-retinal changes secondary to laser therapy can be determined in detail. Be it macular grid or panretinal photocoagulation, for the first time it is possible to visualize intra-retinal morphological changes secondary to laser treatment in the human retina in vivo and to observe their changes over time. All in all, OCT still is a new diagnostic tool improving the insight into the nature of AMD/DM and therapeutically induced effects on retinal morphology. Information about the amount and the location of disease, the extent of retinal damage and the level of lipid exudation visualized by OCT is important to diagnose and manage this complex disease. Together with fluorescein angiography it enables the clinician to choose and follow-up the ideal treatment option in each individual patient, be it surgery, laser therapy or an intravitreally administered agent.

**Questionnaire:**
Which answer is not correct:

a) intraretinal fluid accumulation is documented  
b) subretinal fluid is identified  
c) the nature of the vascular abnormality is identified  
d) intraretinal lipids are detected.

**AVASTIN VS LUCENTIS VS OTHERS: WHAT ABOUT VEGF-TRAP?**  
U. Schmidt-Erfurth  
Austria

Intravitreal bevacizumab as well as ranibizumab have revolutionized the therapy of neovascular age-related macular degeneration (AMD). Both compounds efficiently inhibit the intraocular VEGF in neovascular age-related macular degeneration. Improvements in visual acuity in treated patients are significant and the therapy has become a first line treatment. However, all clinical trials and the experience in clinical practice have highlighted a necessity to monitor patients on a monthly base and to inject every month to obtain optimal results. This has led to a significant dilemma in patient management worldwide. VEGF-trap is another anti-VEGF agent with the design of a fusion molecule. The affinity of this designed substance as well the bioavailability is hypothetically superior to the two other drugs. Primary results of two phase III studies using intravitreal VEGF-trap eye compared to ranibizumab in patients with neovascular AMD (VIEW 1 and VIEW 2) have provided excellent results in the US study (VIEW 1) showing best visual outcome in a monthly regimen which was superior to a monthly ranibizumab regimen. In both trials, VIEW 1 and VIEW 2, VEGF-trap eye provided non-inferiority of a two monthly regimen with VEGF-trap as compared to a monthly regimen with ranibizumab. The proportions of patients maintaining vision with VEGF-trap were 95/96%. Mean improvements ranged between 7.6 and 9.7 letters. There were no concerns regarding systemic safety and the rate of adverse events was low. The proven efficacy of a two monthly regimen has the potential to reduce the frequency of re-injections substantially during long-term follow-up and establishes a new paradigm in the treatment of AMD with entire VEGF substances.

**Questionnaire:**

- It is applied topicaly as eye drops  
- It is injected in quarterly intervals  
- Is superior to the standard therapy with Lucentis in a fix monthly regimen  
- It Consists of a biodegradable implant and obtains non inferior results to monthly ranibizumab in a two monthly fixed regimen.

**VEGF-trap offers a novel perspective in the treatment of neovascular AMD because**

a) It is applied topicaly as eye drops  
b) It is injected in quarterly intervals  
c) Is superior to the standard therapy with Lucentis in a fix monthly regimen  
d) It Consists of a biodegradable implant and obtains non inferior results to monthly ranibizumab in a two monthly fixed regimen.

**STRUCTURE-FUNCTION CORRELATION OF THE HUMAN CENTRAL RETINA**  
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**Background:** The impact of retinal pathology detected by high-resolution imaging on vision remains largely unexplored. Therefore, the aim of the study was to achieve high-resolution structure-function correlation of the human macula in vivo.

**Methodology/Principal Findings:** To obtain high-resolution tomographic and topographic images of the macula spectral-domain optical coherence tomography (SD-OCT) and confocal scanning laser ophtalmoscopy (cSLO), respectively, were used. Functional mapping of the macula was obtained using fundus-controlled microperimetry. Custom software allowed for co-registration of the fundus mapped microperimetry coordinates with both SD-OCT and cSLO datasets. The method was applied in a cross-sectional observational study of retinal diseases and in a clinical trial investigating the effectiveness of intravitreal ranibizumab in macular telangiectasia type 2. There was a significant relationship between outer retinal thickness and retinal sensitivity (p<0.001) and neurodegeneration leaving less than about 50 µm of parafoveal outer retinal thickness completely abolished light sensitivity. The functional preservation was found if neurodegeneration spared the photoreceptors, but caused quite extensive disruption of the inner retina. Longitudinal data revealed that small lesions affecting the photoreceptor layer typically precede functional detection but later cause severe loss of light sensitivity. Ranibizumab was shown to be ineffective to prevent such functional loss in macular telangiectasia type 2.

**Conclusions/Significance:** Since there is a general need for efficient monitoring the effectiveness of therapy in neurodegenerative diseases of the retina and since SD-OCT imaging is becoming more widely available, surrogate endpoints derived from such structure-function correlation may become highly relevant in future clinical trials.

**SHAKEN BABY SYNDROME: OCULAR AND ASSOCIATED SYSTEMIC FINDINGS, MEDICAL AND SURGICAL MANAGEMENT, AMBLYOPIA PREVENTION**  
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Traumatic sequelae of nonaccidental injuries occurring in infants and young children as a consequence of violent shaking are called shaken baby syndrome. Synonyma are whiplash shaken infant syndrome, battered child syndrome or child abuse syndrome. It commonly results in intracocular and intracranial hemorrhages. As the mortality rate is 15% it is important to recognize this form of child abuse. The typical victim of shaken baby syndrome is a male infant younger than six months of age who is alone with the perpetrator at the time of injury. The injury is unrelated to race, gender, socioeconomic status, or education. An infant is more likely to suffer from intracranial and intracocular bleeding as a result of shaking, because the head is proportionately larger and heavier relative to the body than that of an older child or adult and is stabilized less well by neck muscles. The condition is still underdiagnosed to a significant extent: Less than 5% of abused children become known to the authorities. On the other
A 50% incidence of gaze disorders is reported in shaken baby syndrome. As a proportion of these visual losses is related to secondary hemorrhage, which may contribute through a mechanism of nerve fibre compression to the development of optic atrophy in children. Complete clearing, to severe visual loss (secondary to optic atrophy) usually occurs in 11-23% of all physically abused children and in 50-80% of shaken babies. Indirect ophthalmoscopy shows intraretinal hemorrhage in various locations - subretinal, intraretinal, preretinal, and subhyaloid - and intravitreal, concentrated in the posterior pole region and usually bilateral.

The amount of intraretinal blood correlates with the degree of acute neurologic damage. Cotton-wool spots, white-centered hemorrhages, macular edema, papilledema, and retinoschisis are less common. Computed tomography or magnetic resonance imaging detects thrombosis in infants. Retinal hemorrhages are mostly seen post partum or in shaken babies. 24 hours after a normal birth, 19 to 32% will have varying degrees of retinal hemorrhages. Retinal hemorrhages occur in 11-23% of all physically abused children and in 50-80% of shaken babies. Direct ophthalmoscopy shows intraretinal hemorrhage in various locations - subretinal, intraretinal, preretinal, and subhyaloid - and intravitreal, concentrated in the posterior pole region and usually bilateral.

The diagnosis of child abuse requires a high index of suspicion. Child abuse is usually not reported on. Characteristically a history of shaking is lacking. In addition, the shaken infant may present with minimal external signs of trauma. In child abuse, the eye is involved as presenting sign in 4-6% of cases. While after accidental head injuries nearly all babies (≥3 years of age) had normal funduscopic examinations, the majority of babies with nonaccidental head injuries were found to have varying degrees of retinal hemorrhages. Retinal hemorrhages occur in 11-23% of all physically abused children and in 50-80% of shaken babies. Indirect ophthalmoscopy shows intraretinal hemorrhage in various locations - subretinal, intraretinal, preretinal, and subhyaloid - and intravitreal, concentrated in the posterior pole region and usually bilateral.

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The clinical course of shaken baby retinopathy ranges from complete clearing, to severe visual loss (secondary to optic atrophy), or macular scarring. Postmortem examination of the optic nerves in shaken babies often reveal perineural hemorrhage, which may contribute through a mechanism of nerve fibre compression to the development of optic atrophy in survivors. A 50% incidence of gaze disorders is reported in shaken baby syndrome reflecting nervous system insults. Even without evidence for retinal damage visual disturbance may occur. In 1958, Hebbel reported visual loss in 23% of 35 children with subdural or subarachnoidal hemorrhage who showed no evidence of retinal damage. As a proportion of these visual losses is related to secondary amblyopia, it is mandatory to carefully observe the victim regularly to prevent the development of an amblyopia.

Two major mechanisms are involved in Choroidal NeoVascularization (CNV); vessel leakage /CNV proliferation and inflammation. The target of treatment of exudation in Age-related Macular Degeneration (AMD) is presently VEGF. Antibodies directed against that factor are the current way to block VEGF isoforms. A potential treatment at the moment in a phase III trial is VEGF-Trap. This fusion protein of the extracellular portions of VEGF receptor R1 and R2 acts like a soluble receptor of high affinity for all isoforms of VEGF-A. VEGF mRNA or VEGF R1 mRNA decrease the production either of all isoforms of VEGF or of VEGF R1. Two siRNAs have terminated a phase II trial but will not proceed to phase III. The way of administration of all these compounds is by intravitreal injection as the antibodies. Oral, subtenon or local administration is considered for ProTein Kinase (PTK) inhibitors. The PTK especially the isoform PKCβ2 play a major role in the cascade of intracellular reactions stimulated by VEGF. Vatalanib (PTK787), I'AG-013958, I'AL-3924 and TG1010901 are PTK inhibitors evaluated in phase III. Other angiogenic and inhibitor factors may be targeted. For example, Pigment Epithelium-Derived Factor (PEDF) is a natural inhibitor of angiogenesis. Genetically engineered cells may assure a large production of the desired molecule, here PEDF, in the target tissue for a long period of time. A phase III study is in progress to evaluate the safety of IVT or sub tenon administration.

A number of data support the implication of the inflammation pathways in AMD. The easiest way to control inflammation is the use of steroids. Triamcinolone has not yet provided convincing hemorrhage results. Some nonsteroidal anti-inflammatory drugs have been suggested. The biodegradable implant of Posudrel allows a progressive drug delivery. A phase III randomized trial is under the way. An even longer acting non biodegradable implant charged with Fluocinolone Acetonide is also a possible candidate. The complement pathway is concerned by AMD i.e. polymorphism of C3 gene was detected in association with AMD. POT-4 is a synthetic peptide that tightly binds to complement component C3. The inhibition of C3 or C5 effectively shuts down all downstream complement activation such as local inflammation, tissue damage and upregulation of angiogenic factors (i.e VEGF). This new avenue is presently the object of tremendous interest.

The immediate goal of treatment in exudative AMD is to decrease the leakage-induced damage and to limit the progression of the CNV. The inhibition of inflammation could have an earlier impact on the prevention of AMD, on the treatment of the neovascular and possibly atrophic complications.

THE ROLE OF ADJUNCTIVE TREATMENT IN AMD TREATMENT: ADJUNCTIVE THERAPY IS NOT NEEDED

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Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss in the developed world among people over 50 years of age. Intravitreal ranibizumab was the first therapy for exudative AMD to show in two Phase III clinical studies an improvement in mean visual acuity. These results were obtained by a fixed-dosing regimen of ranibizumab 0.5 mg or 0.3 mg monthly injected over 24 and 12 months, respectively. The PrONTO Study assessed a variable dosing regimen mainly based on optical coherence tomography (OCT)-findings. Patients received 0.5 mg intravitreal injections of ranibizumab 0.5 mg and were then evaluated monthly for treatment. Retreatment with ranibizumab was performed at each monthly visit if any criterion was fulfilled such as a loss of 5 letters or more, or any qualitative increase in the amount of fluid was detected on OCT. The PrONTO Study demonstrated variable-dosing regimen to be as effective as a fixed-dosing regimen in improving visual acuity and OCT-findings with a far lower number of injections over a period of 12 and even 24 months. Recently, we published similar results about the 24-month outcomes of intravitreal ranibizumab injections for CNV secondary to AMD in a single-center institutional setting (PRN variable-dosing regimen). In the MARINA trial, the ANCHOR trial and the PrONTO study, the
final mean BCVA at 24 months improved by 7.2, 11.3 and 11.1 letters, respectively. In our study, mean BCVA at 24 months improved by 6.5 letters suggesting comparable results with previous studies.

However, some “real life” studies report a modest effect of anti-VEGF. We believe that the gradual spacing out of follow-up examinations is responsible for the discrepancy between our results and some “real life” papers. Similarly, studies based on quarterly follow up did not achieve such improvement of mean BCVA. The monthly follow-up appears to be the common feature in studies achieving the best final visual acuity. To date, there is no consensus in the literature for a beneficial effect of adjunctive therapy in exudative AMD, neither for type 1, type 2, nor type 3 CNV. On the opposite, PDT remains a strong therapeutic option in polypoidal vasculopathy.

Nevertheless, a wide range of response to anti-VEGF exists among wet AMD patients. A major challenge in the coming next year will be to determine predictive factors for response to anti-VEGF agents. It remains possible to foresee therapeutic strategies, including adjunctive therapies, when such predictive factors will be clearly established. Personalized medicine is on the way and will help to establish approaches based on predictive prognosis factors.

In conclusion, monthly examination of the patients and treatment if any doubt about exudative signs, allow results similar to Marina and Anchor studies without any adjunctive therapy.

**DSEAK VS. CATARACT SURGERY ALONE IN PATIENTS WITH FUCHS' DYSTROPHY**

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The author has no proprietary or financial interest in the products discussed in this paper.

Fuchs' corneal dystrophy is a dominantly inherited, progressive disorder that affects corneal endothelium. It is usually first observed in patients older than 50 years of age but can be seen in some patients in childhood. There is a progressive loss of endothelial cells with a secretion of an abnormally thickened basement membrane, leading to guttata formation. These guttata are often best seen by retro illumination but can be seen by direct illumination of the slit lamp.

Cataract surgery in patients with Fuchs’ corneal dystrophy presents a challenge, because the intracoronal surgery can result in an 8%-10% loss of the endothelial cells. The use of dispersive viscoelastics may lessen endothelial cell loss during surgery.

The decision as to whether to perform cataract surgery alone or cataract surgery plus Descemet stripping automated endothelial keratoplasty (DSEAK) is often complex and depends on the assessment of endothelial cell health. It is debated whether the best assessment is by endothelial cell counts or central corneal pachymetry. In our practice we have found endothelial cell counts to vary significantly and not be helpful in determining when a cornea with Fuchs' endothelial dystrophy might decompensate with a cataract surgery. Therefore, we rely on clinical appearance of the cornea (epithelial edema vs. no edema), the pachymetry measurements of the cornea, and the visual needs of the patient.

Past publications, including the Preferred Practice Pattern® Basic and Clinical Science manual for ophthalmologists, have indicated that a preoperative corneal thickness of >0.60 mm (600 µm) may be predictive of corneal decompensation, and indicates that an initial penetrating keratoplasty may be required in these patients in combination with cataract surgery. Our experience at the Wilmer Eye Institute indicates that many patients with a preoperative corneal thickness of >600 µm, as measured by pachymetry, do very well after cataract surgery and do not require postoperative penetrating keratoplasties or DSEAK.

We recently published in “Ophthalmology” a twelve year review of 136 patients with Fuchs' dystrophy who underwent phacomulsification and intraocular lens implantation. The average preoperative corneal thickness in these was 580 µm, and fifty eyes (36.8%) had preoperative corneal thickness ≥600 µm. Postoperatively the average visual acuity of our patients 20/33. None of the eyes with a preoperative corneal thickness of <600 µm decompensated within two years after cataract surgery. Of the fifty patients with preoperative corneal thickness measurements of greater than or equal to 600 µm, only 5 (10%) progressed to penetrating keratoplasty and 90% of the fifty eyes did not need a corneal transplant at least within the first one to two years after cataract surgery. These patients had an average visual acuity of 20/35 postoperatively. Based on these results, we have suggested that the preferred practice pattern for ophthalmologists extend the indications for cataract surgery in patients with Fuchs’ dystrophy without obvious epithelial edema to undergoing cataract extraction without keratoplasty if the corneal thickness is >640 µm. A study recently published in the American Journal of Ophthalmology indicated that they have an approximately 10% chance of needing a keratoplasty within the first one to two years after surgery and if they live long enough they may eventually need a PK or DSEAK, because this is a progressive disorder. We modify our viscoelastique use during surgery in patients with Fuchs’ dystrophy to use a dispersive viscoelastic such as Viscoat or Healon 5 to offer better protection of the endothelium during the phacoemulsification portion of the surgery. No study has been performed to definitively show that this is beneficial, but it is our belief that a dispersive viscoelastic helps protect the endothelium from the disadvantage of the dispersed viscoelastic that it may trap small nuclear fragments in the peripheral angle that are not removed during phacocentrification and/or irrigation-aspiration of the remaining viscoelastic. The retention of small nuclear fragments in the anterior chamber angle after cataract surgery can be damaging to endothelium and cause corneal decompensation of the cornea. Therefore, one must be very careful to remove all nuclear chips during the cataract extraction and/or irrigation-aspiration.

Our teaching in the past has been to perform cataract extraction alone in patients with a Fuchs' dystrophy and a central corneal thickness of ≤640 µm. We realize that an increase in corneal thickness does lead to increase in light scatter and have found in our studies that as the corneal thickness goes above 640 µm, visual acuity begins to deteriorate. We also reported on 12 patients who had a central corneal thickness between 640 µm to 680 µm, who underwent very careful cataract surgery. These were elderly and/or one eyed patients whom we thought penetrating keratoplasty or DSEAK was not warranted. Ten of the 12 cases (86%) maintain clear corneas at two years after surgery, with a median visual acuity of 20/40. There seems to be a correlation of increased corneal thickness of over 640 µm with a decrease in visual acuity, and currently we are evaluating this in a large number of Fuchs’ dystrophy patients after cataract surgery. Certainly if a patient has a corneal thickness between 550 µm and 640 µm with epithelial edema that cornea has decompensated and a PK or DSEAK is indicated. We can determine epithelial edema by retro illumination view and/or applying a cotton tip applicator to the cornea after using anesthesia to see if it is detached indicating epithelial edema.

The recent developments and popularization of DSEAK by Mellis®5, Terri®6,7,8,9,10 will certainly decrease the number of PK’s for Fuchs’ corneal dystrophy. We still recommend a simple cataract operation if there is no epithelial edema and central corneal thickness is <640 µm. This in many of our patients has provided 20/20 visual acuity with a 90% chance of not needing a corneal transplant. If there is epithelial edema, and when the corneal thickness goes above 640 µm there will be decreased visual acuity due to light scatter from the stroma and epithelial edema. In these cases we are now recommending a combination of phacomulsification and DSEAK to prevent further damage of the cornea, and we have done 12 cases of this procedure. Currently we are doing a prospective study in 20 patients with a median central corneal thickness of 640 µm to 680 µm and a median visual acuity of 20/40. If there is not an improvement, a PK or DSEAK is recommended to prevent further damage of the cornea. We have 12 cases of this procedure and we have not seen any cases with epithelial edema that would require penetrating keratoplasty. In our experience the endothelial cell loss with DSEAK is less than with PK, as the incidence of dislocation and rejection has recently dropped less than 10% of our cases with PK and DSEAK.

Although DSEAK is becoming more popular, there are limitations to this procedure. A recent report in Ophthalmology indicates that 10-15% of DSEAK’s dislocate. Our percentage of dislocation is less than 5%. Terri®6,7,8,9,10 recently reported less than 2% dislocation. We have seen two cases in forty with rejection, and both of these have cleared.
In summary, we have extended the indications for cataract surgery without simultaneous corneal endothelial replacement surgery in eyes without epithelial edema to a corneal thickness of 560 µm and possibly to 600 µm. The ability to perform DSAEK, which is less debilitating to the patient than PK, has encouraged us to extend the indications for cataract extraction in patients with moderate Fuchs’ dystrophy but without epithelial edema, realizing that DSAEK can be performed later if the patient does not achieve adequate visual acuity with cataract surgery alone. Since the DSAEK operation induces about -1.50 diopters hyperopic shift we aim for a postoperative spherical equivalent of -1.50 to 1.75 diopters in patients undergoing combined DSAEK and cataract extraction or in Fuchs’ patients who are undergoing cataract surgery and may need a later DSAEK.

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MULTIFOCAL IOL’S

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Recent trends in cataract surgery indicate a growing demand for advanced technology intraocular lenses. It is estimated that by 2015, the number of patients over 60 will increase as of percentage of the overall population, generating more increased demand for cataract surgery. Of these patients, there will be a significant number who will desire presbyopia correction at the time of surgery. The most popular methods of correcting presbyopia in cataract surgery are multifocal and accommodative intraocular lenses. The most preferred multifocal IOL is the apodized diffractive Acrysof® IQ ReSTOR® +3.0D IOL. The ReSTOR® lens has been designed to offer good performance at all distances by delivering near, intermediate and distance vision. The Tecnis multifocal IOL is also FDA approved and provides +4 diopter addition closer reading distance than the Restore IOL. The most preferred accommodating IOL is the Crystalens. While both lens technologies are designed to reduce spectacle dependence following cataract surgery, recent studies indicate that multifocal lenses may provide greater spectacle independence, better predictability and enhanced near visual acuity. This presentation will discuss current market trends in the advanced technology IOL market. It will review the market leading multifocal IOL technology and compare the performance of these lenses to the most preferred accommodative IOL technology.

PROGRESSION OF AGE-RELATED MACULAR DEGENERATION AFTER CATARACT SURGERY

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Objective: To document age-related macular degeneration (AMD) progression after cataract surgery.

Methods: Surgeons prospectively enrolled patients with nonneovascular AMD who were awaiting cataract surgery. Fluorescein angiography was performed preoperatively and at the postoperative week 1, month 3, and month 12 visits. Incidence of neovascular AMD development within 12 months after operation was the primary outcome measure.

Results: A total of 108 subjects were enrolled. Of 86 eyes with preoperatively photographically confirmed nonneovascular AMD, 71 hadgradable images by month 12. Neovascular AMD was observed in 9 of 71 eyes (12.7%; 95% confidence interval, 6.0%-22.7%). The progression rate between week 1 and month 12 decreased to 3 of 65 eyes (4.6%; 95%confidence interval, 1.0%-12.9%) after excluding 5 neovascular events identified on the postoperative week 1 visit and 1 case with missing photographs at this visit.

Conclusion: The low incidence rate of neovascular AMD development between 1 week and 1 year after cataract surgery did not support the hypothesis that cataract surgery increases the risk of AMD progression. Several eyes appeared to have disease progression on postsurgery week1 fluorescein angiograms, suggesting that many cases of presumed progression to neovascular AMD follow cataract surgery may have been present prior to cataract surgery, but not recognized owing to lens opacity.


SURGICAL TECHNIQUE FOR SUTURE FIXATION OF AN ACRYLIC INTRAOCULAR LENS IN THE ABSENCE OF CAPSULE SUPPORT

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Inadequate capsule support is a rare but potential complication associated with cataract surgery. Options include leaving the patient aphakic, placing an anterior chamber (AC) intraocular lens (IOL), or suture-fixating a 3 piece foldable acrylic IOL in the ciliary sulcus or the peripheral iris. We now prefer suturing the IOL to the peripheral iris using a modified McCannel technique.

The technique can be accomplished through a 3.5mm central incision. The pupil is constricted with acetylcholine to facilitate papillary capture of the IOL optic. The IOL is folded in a “moustache fold” and inserted through the corneal wound, placing the haptics within the sulcus and positioning the optic above the plane of the iris (Figure 1). A Barraque sweep is passed through the paracentesis and placed beneath the optic as the lens is unfolded. Additional viscoelastic material is injected into the AC, pushing the iris posteriorly against the haptics. The Barraque sweep is used to elevate the optic. Both maneuvers facilitate visualization of the haptics, simplifying passage of the sutures. Using a modified McCannel-type iris fixation technique, a 10-0 polypropylene (Prolene®) suture is passed on a needle (Ethicon CTC-6) through clear cornea and the iris, under the peripheral aspect of the inferior haptic, then out through the iris and clear cornea (Figure 2). A paracentesis is created over the inferior haptic, and two ends of the suture are pulled through this site (Figure 3). The superior haptic is secured in a similar manner. The sutures are loosely tied with a single throw (Figure 4) and are not locked. The optic is placed posterior to the iris. Using a Sinskey hook, the iris is manipulated to produce a round pupil (Figure 5). Microlol is injected again to ensure a round miotic pupil (Figure 6-7). The sutures are securely tied.

If there is no capsular support the sutures are tied tight before the optic is placed in the posterior chamber. If necessary, a vitrectomy through a pars plana incision or an anterior vitrectomy through the corneal wound is performed. The retained viscoelastic material is removed from the AC. Air is injected into the AC and checked for unidentified strands of vitreous. If vitreous is present, a Barraque sweep is used to break the strands or a more extensive vitrectomy is performed.
Then, a repeat injection of air is made into the AC, again inspecting for vitreous. A balanced salt solution is injected into the AC, bringing the eye to a more normal physiologic pressure. The wound is tested for leaks.

The ability to insert and suture-fixate an IOL through a 3.5 mm incision gives the surgeon greater flexibility in treating patients with no capsule support. This technique permits secondary IOL insertion in aphakic patients who are contact lens intolerant, facilitates the management of IOL problems after surgery that require IOL exchange, and allows the surgeon to properly treat patients who develop loss of capsule support at the time of cataract surgery.

References

Figure 1A    Figure 1B       Figure 1C
Figure 1D    Figure 1E       Figure 1F
Figure 2    Figure 3        Figure 4
Figure 5    Figure 6        Figure 7

TREATMENT OF ARN - THE IMPORTANCE OF SURGICAL TREATMENT, INCLUDING LASER
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Acute retinal necrosis is a syndrome of necrotizing retinal vasculitis that was first described in Japan in the 1970’s and further characterized across the world in the 1980’s. It is now thought to be caused by a herpesvirus, most often varicella zoster. Most patients with ARN are immunocompromised, although a more severe form, Progressive Outer Retinal Necrosis or PORN, can occur in AIDS patients. ARN begins with symptoms of a mild uveitis, but careful examination of the retinal periphery will often reveal areas of patchy retinal whitening with splotchy intraretinal hemorrhages. Over time, these patches will become confluent and spread posteriorly, with progressively increasing vitritis and, in some cases, optic neuritis. Untreated, retinal detachment is common, with the inflammation inducing a posterior vitreous detachment leading to large retinal tears in areas of necrotized tissue.

The mainstay of therapy for ARN is the use of antiviral therapy, including intravitreal acyclovir, intravenous acyclovir, and oral valacyclovir. If the diagnosis is made early enough in the course of the disease, the condition will respond rapidly to the medication, with the involved tissue showing granular hyperpigmentation. The subsequent addition of corticosteroids may promote resolution of the vitritis. However, severe vitreous loss may still ensue from retinal detachment. Surgical intervention, including laser, has been advocated with three goals: 1) Diagnostic vitrectomy to assist in diagnosis, 2) Prophylactic laser with or without vitrectomy to reduce the chance of retinal detachment, and 3) Vitrectomy to treat eyes that develop retinal detachment.

Diagnostic vitrectomy. Vitreous biopsy can play an important role in confirming the suspected diagnosis of ARN. Vitreectomy has been used to assist with diagnosis in ARN since the 1980s. At that time, prior to the determination of the viral etiology, vitreous specimens underwent bacterial, fungal, and viral culture, but were unsuccessful in identifying a causal organism.

In addition, the vitreous wash was examined by cytopathology; inflammatory cells were seen but there was no pattern detected that was compelling with regard to pathogenesis. Some surgeons attempted retinal biopsies; ultimately Cubertson and colleagues identified viral elements on electron microscopy on two autopsy eyes consistent with a herpes group virus.

The emergence of PCR has assisted greatly the potential benefit of diagnostic vitrectomy. A 2010 study from Japan of 30 eyes suspected of ARN showed that vitreous biopsy with PCR detected varicella zoster in 26 eyes, herpes simplex virus in 5 eyes, and EBV in 2 eyes. In 2007, Lightman and colleagues in England has reported similar findings, identifying VZV in 12/18 eyes, HSV in 4/18 and EBV in 3/18. In both studies, VZV was also detected in all eyes positive for EBV.

Prophylactic laser and vitrectomy. Given the greater than 50% risk of retinal detachment in eyes with ARN, prophylactic laser was first advocated in the late 1980s. It had been noted that when RDs occurred in ARN, the retinal tears often occurred at the border of involved (or necrotic) and uninvolved (or healthy) retina. It was hypothesized that several rows at laser placed just posterior to the intersection could provide a stronger adhesion, decreasing the risk of retinal tearing when the vitreous separated and pulled at the weakened necrotic tissue.

Several studies showed a significant reduction in rate of retinal detachment comparing eyes that received such laser versus those that did not. These studies were criticized, with the suggestion that many more advanced cases could not receive prophylactic laser because severe vitreous debris precluded adequate visualization. Thus, the lower rate of RD in the lasered eyes was the result of these being milder cases, rather than due the benefit of the laser.

However, a 2008 editorial questioned further the benefit of prophylactic laser, noting the heterogeneity of the populations studies in published reports. While some surgeons continue to downplay the importance of prophylactic laser, a 2010 study from Chicago reviewed their 20 year history with ARN and showed no eyes with prophylactic laser developed RDs. On the other hand, a retrospective study from Boston published in 2010 noted that no variables, including prophylactic laser photoagulation, were associated with reduced risk of retinal detachment. The authors of the 2008 editorial suggest a multicenter, prospective, randomized, controlled study, but the limited number of cases make such a trial unlikely.

There is even more controversy over the potential benefit of prophylactic vitrectomy. Early vitreous surgery has been advocated as a means for reducing vitreoretinal traction, removing vitreous debris to facilitate prophylactic laser, and for antiviral lavage. While there are studies that have demonstrated that early vitrectomy with laser can reduce the risk of retinal detachment, no studies have definitively demonstrated improved long term visual outcome with this intervention.

Vitrectomy for retinal detachment. Retinal detachments in the setting of ARN are complex, given the combination of inflammation, necrotic retina, and large tears. As a result, many PCR surgeons agree that vitrectomy is critical to the successful repair of these rhegmatogenous detachments. In addition, it is
common for surgeons to utilized long acting vitreous tamponade as an adjuvant, frequently employing silicone oil. A 2003 study reported successful reattachment in all 18 eyes studied, but noted the need for additional procedures in 13 eyes.

Conclusion. The Acute Retinal Necrosis (ARN) syndrome is a severe form of necrotizing vasocclusice retinitis that occurs predominantly in immunocompetent patients and visual potential is compromised both by retinal damage and retinal detachment. There is compelling evidence that surgical treatment can play an important role in management at the front end, with diagnostic vitrectomy combined with PCR assisting in the diagnosis, and at the back end, with vitreoretinal surgical techniques valuable in the repair of the ensuing complex retinal detachments. While there is controversy over the role of prophylactic laser and/or vitrectomy, substantial evidence supports their serious consideration.

PRONE POSITIONING AFTER VITRECTOMY FOR MACULAR HOLE: IS IT NECESSARY - CON: PRONE POSITIONING IS NOT NECESSARY

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Background. Prior to the 1990’s, idiopathic macular hole was considered an inoperable condition. In 1991, however, Kelley and Wendel published their landmark paper demonstrating the efficacy of initial surgery, macula plana vitrectomy, with separation of the posterior hyaloids, fluid-gas exchange, and postoperative face down positioning. In this report, they were able to close 58% of macular holes successfully. In subsequent years, there have been a number of refinements proposed. These have included the use of adjuvants, such as TGF-beta or autologous serum, varying the intraocular tamponade, using silicone oil or air rather than sulfur hexafluoride, and performing peeling of the internal limiting membrane in addition to the separation of the hyaloids. Almost regardless of the technique used, most studies report anatomic closure rates of greater than 90%.

“The Case” In addition to the surgical modifications noted above, there has also been discussion about the optimal duration for postoperative prone positioning. Reports have ranged from suggesting only 3 days to up to 2 weeks. However, as early as 1997, Tomnabe and colleagues posited that facedown positioning may not be necessary at all. They reported 33 eyes managed by vitrectomy, ILM peeling and SF6 insufflation and no period of prone positioning. Successful hole closure was achieved in 75% of eyes, comparable to what was being achieved with lengthy face down positioning in that decade. Yet this management was largely ignored by surgeons worldwide.

Certainly, prone positioning is highly inconvenient for all patients and physically quite challenging for the elderly, for obese patients, for those with prólapse of the rectus muscles, and those with breathing difficulties such as sleep apnea. Further, prone positioning can be challenging for individuals that live alone or have limited support systems. Thus, the demonstration that macular hole closure can be achieved without face down positioning would be highly advantageous.

In Machemer’s seminal Jackson Lecture on mechanism of retinal detachment, he stated that a rhegmatogenous detachment could be repaired by removal of vitreous traction on the retinal hole and reduction in fluid movement. Thus, theoretically, a macular hole and associated localized detachment should be repairable with vitrectomy and ILM peeling and intraocular gas without the need for face down positioning. The efficacy of this has been demonstrated by OCT studies, showing that the edges of the macular hole become opposed as soon as one day after surgery.

“The Evidence” Thus, a number of surgeons have reported results from both consecutive series of patients managed with shorter duration prone positioning and comparative series of patients managed with different durations. The most comprehensive review of the evidence supporting prone positioning is a meta-analysis by Tatham and Banerjee published in 2010. They identified 17 studies relevant to the question at hand, but only 9 where there was a comparison group. Five studies compared macular hole surgery with prone positioning for 24 hours or less versus 5-10 days. In all 5 studies, the hole closure rate was similar in the two groups (around 90%). There was limited data on vision improvement in all but one study. Four studies compared surgery with 3-7 days prone positioning versus 7-28 days. In three of the studies, the closure rate was comparable between the two group. In one study, which used TGF-Beta as an adjunct, the shorter duration group had a significantly lower rate of the edge however the 3 day group had air use as tamponade versus 16% C3F8 in the 21 day group. Perhaps the largest relevant study is one reported by Guillaube et al. This group found no significant difference in closure rate for smaller holes, but a lower rate in larger holes (larger than 400microns) managed without face down positioning.

Conclusion. Overall, the authors of the meta analysis concluded that there is limited evidence to support the importance of face down positioning following macular hole surgery.

COMBINED ANTERIOR AND POSTERIOR SEGMENT TRAUMA

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Ocular trauma is a leading cause of monocular blindness, with an estimated half million blinding ocular injuries worldwide each year.

Closed Globe Injuries. Closed globe injuries can affect both the anterior and posterior segment. Manifestations of closed globe trauma include traumatic hyphema, lens subluxation and dislocation, vitreous hemorrhage, commotio retinae, avulsion of the vitreous base, retinal tear, macular hole, retinal detachment, traumatic optic neuropathy, and optic nerve avulsion. While some of these injuries can lead to devastating irreversible vision loss, most do not require urgent intervention, but rather full evaluation and thoughtful management. It is critical to monitor IOP in the setting of hyphema, and to perform ultrasonography to look for retinal detachment when visualization of the retina is impaired.

Open Globe Injuries. On the other hand, open globe trauma often necessitates emergent surgery. It is important to obtain a history and perform as complete an exam as possible to determine the extent of the injury and to prepare properly for surgery. Important prognostic factors include visual acuity and the presence or absence of an afferent papillary defect.

Primary Repair. The first step in managing an open globe injury is repair of the laceration or rupture. The goals are to restore the structural integrity of the globe, with watertight closure of all wounds and restoration of normal IOP, protecting the visual axis if possible, and avoiding iatrogenic damage. Before repairing the laceration, it is critical to determine the extent of the injury. Repairs should be performed with normally starting at the site of injury, and working posteriorly. If an injury crosses the limbus, it is easiest to first reapproximate the tissue at this location. Incarcerated tissue should be repositioned when possible, unless it appears extremely necrotic. If it is apparent that a sclera laceration is present, a penetrating injury should be performed and the sclera explored carefully to determine if the laceration is either located or extending under the rectus muscles. If vitreous has extended through the laceration, it should be cut with a sharp scissors flush with the sclera. The value of sclera buckling surgery at the time of primary repair is controversial. Several studies suggest this may be beneficial by supporting the vitreous base, reducing vitreoretinal traction, and reducing the risk of subsequent retinal detachment.

Intraocular Foreign Bodies. Intraocular foreign bodies (IOFBs) should be removed at the time of repair of the entry site or soon afterward, both because they rapidly become encased in a fibrous capsule, and because they have a higher association with traumatic endophthalmitis. Most IOFBs will require pars plana vitrectomy for removal, whether magnetic or nonmagnetic. Extremely large foreign bodies, such as BB pellets, can pose great difficulty for the surgeon.

Lens damage. Management of cataract after penetrating injury is controversial, with some advocating primary lensectomy and others suggesting a second procedure. In more severe injuries,
lens removal may be necessary for visualization of the posterior segment so as to remove a posteriorly located IOFB or repair a retinal detachment. If the injury is limited to the anterior segment, or if there is deferred need for surgery following primary repair permits clearing of fibrin and inflammation and allows proper determination of lens position, capsular integrity, and IOL power.

Role for vitrectomy. Despite advances in management of eyes with penetrating injuries, the eyes with more severe injuries involving the posterior segment still carry a poor prognosis. Vitreous surgery is often indicated in this setting, however it is controversial as to whether it should be performed at the time of the primary repair or deferred 7-10 days to allow further diagnostic evaluation, reduction in inflammation, and clearing of anterior segment hemorrhage. Early vitreous surgery is encouraged for eyes with IOFBs, endophthalmitis, and obvious retinal detachment. Deferred vitrectomy may be beneficial otherwise; however, most authors believe that such surgery should not be delayed beyond 14 days.

Once the decision has been made to perform a vitrectomy, surgical goals include clearing the ocular media through removal of cataractous lens or vitreous hemorrhage, removing the vitreous scaffold from the laceration site, removing the posterior hyaloids that could provide a future scaffold for vitreoretinal traction or epiretinal membrane formation, removal of any IOFBs, and identifying and treating retinal breaks and detachment. From the onset of the case, the surgeon will be making critical decisions that can have a profound influence on outcome, including management of preexisting hemorrhagic choroidal detachment, management of anterior segment hemorrhage and cataract, and placement of the infusion cannula. Management of the posterior segment injury can not be addressed until the anterior segment is cleared. In some cases, severe corneal injury complicates the ability to perform this surgery. Visualization through a scarred cornea can be improved with the use of a wide angle viewing system, but more severe anterior segment injuries may require use of a temporary keratoprosthesis.

Perforating injuries. Perforating injury represents a small subset of ocular trauma, where there is both an entry and exit site. If both sites are easily accessible, they should be closed at the time of primary repair. However, it is more common for the exit site to be inaccessible, in which case the anterior entry site is closed and the posterior exit allowed to close spontaneously. Vitrectomy surgery is delayed for 7-10 days, at which time such surgery is performed to prevent vitreoretinal proliferation.

Conclusion. As the vast majority of ocular trauma is preventable, physicians should emphasize the importance of protective eyewear for all recreational or occupational activities that may lead to eye injury. Protective lenses with polycarbonate spectacles should be prescribed for all individuals who are monocular, regardless of the etiology.

NEAR-INFRARED AUTOFLUORESCENCE

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Autofluorescence (AF) imaging is playing an increasingly important role in the diagnosis of age-related macular degeneration (AMD) and retinal dystrophies. AF is most often generated with short-wavelength excitation (SW-AF) using a confocal Scanning laser ophthalmoscope (SLO). With this imaging mode the signal is dominated by RPE lipofuscin. AF imaging can also be obtained by near-infrared (NIR) excitation. The fluorophore visualized with this imaging modality is melanin, which is found in the RPE, normal retina, and choroid. Melanin also contributes to the NIR-AF signal. This melanin, as well as that in hair and skin, is embryologically derived from the neurocrest and exhibits marked variations with ocular pigmentation. Examples are shown that the NIR-AF signal from the choroid is dependent on the iris color. Other effects such as the loss or oxidation of NIR-AF with age are discussed.

Finally, clinical cases of NIR-AF as age-related, toxic and hereditary macular diseases are introduced.

NIR-AF imaging offers the ability to monitor ocular melanin in vivo. This may help in detecting early degenerative changes of the RPE in patients that are at high risk for the development of age-related, hereditary, or toxic macular disorders.

PLEOMORPHIC ADENOMAS OF THE LACRIMAL GLAND SHOULD BE BIOPSIED

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In 1978, Font and Gamel presented follow-up data of 265 lacrimal gland lesions of which 136 (51.1%) had been classified as benign lacrimal gland pleomorphic adenoma (LGPA), 7 as malignant LGPA arising in LGPA, and 120 as other malignant lacrimal gland tumours. Follow-up (mean, 12.8 years) was available of 113 cases with benign LGPA. The average recurrence rate in this series was 13%. Interestingly, it was only 3% in the group in whom the tumor had been excised intact without a prior biopsy. When a biopsy had been taken, the recurrence rate was 32%, and when the pseudcapsule of the tumor had been damaged during surgery it was 21%. In the group in which a recurrence was excised, the lesion recurred again in 70%. These data thus made a strong case in favor of primary total removal of LGPA without a biopsy and with intact pseudocapsule.

Although, at first glance, this seems a logical conclusion, questions arise. No data are presented regarding the number of cases in which the tumor capsule was (further) damaged during tumor excision in the group who underwent a biopsy. No details are given regarding the applied surgical or biopsy techniques. It is unclear if the biopsy channel was excised. It is surprising that a biopsy is related to a higher recurrence rate than violation of the pseudocapsule during surgery.

In 1979, Wright and co-workers published data on a series of 40 patients with lacrimal gland tumors, of whom 20 suffered from LGPA and 20 of a primary malignant epithelial tumor. This paper presents a breakdown of clinical and surgical data. Although follow-up data are lacking this does not withold the authors from presenting a lengthy discussion that emphasizes the necessity to totally excise LGPA without prior biopsy.

In 1992, Rose and Wright published data on 78 lacrimal gland tumors that were clinically suspected to be LGPA. Of these, 71 had been referred without previous surgery. Of these 71 cases, 55 fulfilled both the clinical and imaging criteria applied by the authors as fitting the diagnosis LGPA. Despite this, the diagnosis later proved wrong in 8 (15%) of these 55 cases. Of the 71 cases, the tumor affected the orbital lobe in 63 cases, and the palpebral lobe in the remaining 8 cases. All 55 tumors were totally excised. With a mean follow-up of more than five years in 92% of cases, no recurrences were found. After excision of the orbital lobe, 25% of the patients suffered from diplopia in extremes of gaze, 25% from filamentary keratopathy and 21% required lubricants. In the cases that underwent excision of the palpebral lobe, the frequency of these side-effects was about three times higher. Data on the total number of patients suffering from one or more side-effects are lacking. We can therefore only conclude that excision of the orbital lobe of the lacrimal gland causes side-effects in more than 25% of patients, while excision of the palpebral lobe causes filamentary keratopathy and other problems in more than 78% of patients. In summary, 55 of these 78 tumors were totally excised, of which 8 with a wrong diagnosis. During follow-up, there were no recurrences in the whole group, including those who underwent a biopsy. While 40% of all cases suffering from LGPA underwent a biopsy and showed no recurrence, and while more than 25% of the patients in whom the orbital lobe of the lacrimal gland was excised suffered side-effects, the authors still reached the remarkable conclusion that a LGPA should be excised without prior biopsy. It is also remarkable that the authors were congratulated with their conclusions in an editorial, while, a few issues later, the authors had to admit that the conclusion that LGPA should be excised without prior biopsy could not be based on their data.
In 1997 Currie and Rose published another series of 133 patients surgically treated for LGPA. In 72 patients, follow-up was at least five years. In the latter group, intact excision had been performed in 46 patients. Postoperatively, attenuated excision of the capsule in 9 underwent open biopsy, 5 had preoperative breach of the pseudocapsule and 5 were operated after previous incomplete excision. During follow-up there was one recurrence, in a patient in whom a biopsy had been taken. The authors conclude that incomplete excision of LGPA predisposes for recurrence. While this conclusion suggests that, consequently, a biopsy should be avoided, the latter conclusion is not substantiated by the presented data.

In a 2009 paper, Rose stated that open biopsy is associated with a 10% chance of tumor recurrence, and that it would be foolish to biopsy a lesion that shows clinical and imaging characteristics of a LGPA. This 10% recurrence incidence proves based on the study described above, in which one out of 72 patients suffered from a recurrence. This patient, as well as nine others, had undergone a biopsy prior to excision. The extrapolation of one recurrence in a subset of nine patients to a 10% chance of recurrence after biopsy in a next paper lacks any statistical justification. The author also remarked that “with rare exceptions, benign tumors of the lacrimal gland are pleomorphic adenomas.” In this sentence, the word “epithelial” is missing. Furthermore, this statement is clinically not very helpful. Lymphocytic infiltration of the lacrimal gland or malignant lacrimal gland tumors are not always easily distinguished from a LGPA and even experienced orbitologists will not adequately diagnose LGPA in up to 22% of cases.

In 1994, Henderson reported on 26 cases of LGPA. In two cases, the tumor capsule was not intact on histological examination. In two other cases, the capsule ruptured during surgery. One other patient had piecemeal removal due to tumor necrosis, and in one other an open biopsy had been performed. In the whole group, no recurrences were seen after a follow-up ranging from 8 to 15 years.

Recently, Lai and co-workers reviewed the literature to find out if what evidence supports the claim that a biopsy should be avoided in LGPA. They concluded that data regarding the recurrence rate after an open biopsy are contaminated by confounding factors, such as incomplete tumor removal or possible spillage of tumor cells, to such extent that no conclusions can be drawn regarding the relation between an open biopsy of a LGPA and the risk of tumor recurrence.

Literature data do however suggest that incomplete excision of LGPA is associated with a higher recurrence rate as compared to complete removal. While this provides some support in favor of total removal of a LGPA without biopsy, the disadvantages of such an approach must also be weighted. As stated above, excision of the orbital lobe of the lacrimal gland will cause side-effects in more than 25% of cases. This percentage does not include any morbidity associated with the lateral orbitalotomy procedure. Without biopsy, the diagnosis LGPA will be wrong in 15-22% of cases. Consequently, these subjects will either be overtreated or undertreated. Although it is unclear to what extent initial undertreatment affects survival in patients with a malignant lacrimal gland tumor we may assume that, by the same token, radical excision of these tumors constitutes the preferred treatment.

The 32% recurrence rate after biopsy of LGPA, as described by Font and Gamel in 1978 has not been reported since. It is therefore, likely that their figure was based on inadequate (contaminated?) data. Nevertheless, the opinion that LGPA should not be biopsied was repeated in literature many times since, and each time without adequate supporting data. Unfortunately, the statement that LGPA should not be biopsied is circular and hence illogical. You don’t need to biopsy a lesion if you know what it is, but you only know for sure what it is after you have taken a biopsy.

Instead of an open biopsy, a fine needle aspiration biopsy (FNAB) can be used. Two authors described good reliability of FNAB in orbital mass lesions, especially when a combination of (immuno)histology and immunocytochemistry is used.

These series, however, provide no precise data regarding how well FNAB will differentiate between LGPA and other lacrimal gland lesions. In conclusion, authorities may present strong opinions that are not based on adequate data but that nevertheless create a mental box from which it proves difficult to escape, for themselves as well as for others. The assumption that LGPA should not be biopsied provides an excellent example of this mechanism. The application of FNAB is promising, but more precise data on its reliability in lacrimal gland lesions are needed.

References

DACRYOCYSTOGRAPHY HAS ALMOST NO ROLE IN THE ROUTINE ASSESSMENT OF LACRIMAL DRAINAGE PROBLEMS
D H Verity
UK
Summary: Imaging is not typically required to reach a diagnosis in patients with lacrimal symptoms, and a careful history often gives the diagnosis. The examination is performed to confirm or refute clinical suspicion, and imaging is only undertaken in selected cases. Thus, the astute clinician infrequently requires lacrimal imaging – of any sort – to form a diagnosis. Only in cases where the clinical history appears not to be supported by the signs (e.g., ‘symptom-signs mismatch’), or where there has been previous injury or surgery, should imaging be considered. Finally, endoscopy should be undertaken in those having undergone previous surgery (endoscopic dye test), as this will give useful information regarding the nasal mucosa, extent of mucus production, and the patency and size of the surgical fistula.

Available imaging modalities:
1. Dacryocystography (DCG): Identifies anatomy (a lacrimal ‘roadmap’)
2. Dacrosintillography (DSG): Investigates dynamic behaviour (physiology)
3. CT: Images adjacent structures
4. DCG-CT: Defines relationship of drainage pathways to adjacent structures

Which patients do need imaging?
1. Children – in cases of failed probing or late presentation
2. ‘Symptom-sign mismatch’ (e.g., intermittent presumed dacrocystitis in the presence of outflow patency may be due to a dacryolith or lacrimal anlage, identified on DCG)
3. Unusual signs (e.g, swelling above the medial canthal tendon, presumed to be neoplasia until refuted on imaging and/or biopsy)
4. Previous lacrimal surgery (a DCG will identify a residual 'sump', a DSG may identify failure of transit to the nose despite patency on syringing - so-called 'functional epiphora')
5. Nasal / midface disease
6. Hereditary – Clefting syndromes
7. Previous trauma or facial surgery